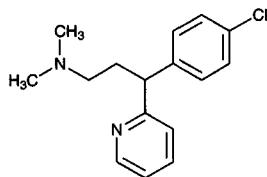


Chlorpheniramine



Molecular formula: C₁₆H₁₉ClN₂

Molecular weight: 274.79

CAS Registry No.: 132-22-9, 113-92-8 (maleate), 2438-32-6 (maleate), 25523-97-1 (d-form), 2438-32-6 (d-form maleate)

Merck Index: 2232

Lednicer No.: 1 77

SAMPLE

Matrix: blood

Sample preparation: 2 mL Whole blood or plasma + 2 mL buffer + 5 mL chloroform: isopropanol:n-heptane 60:14:26, shake gently horizontally for 10 min, centrifuge at 2800 g for 10 min. Remove the lower organic layer and evaporate it to dryness under vacuum at 45°, reconstitute the residue in 100 µL mobile phase, centrifuge at 2800 g for 5 min, inject a 50 µL aliquot of the supernatant. (Buffer was saturated ammonium chloride solution 25% diluted with water, adjusted to pH 9.5 with 25% ammonia solution.)

HPLC VARIABLES

Column: 300 × 3.9 4 µm NovaPack C18

Mobile phase: MeOH:THF:buffer 65:5:30 (Buffer was 0.68 g/L (10 mM (sic)) KH₂PO₄ adjusted to pH 2.6 with concentrated orthophosphoric acid.) (At the end of each session wash the column with water for 1 h and MeOH for 1 h, re-equilibrate for 30 min.)

Column temperature: 30

Flow rate: 0.8

Injection volume: 50

Detector: UV 225

CHROMATOGRAM

Retention time: 5.60

Limit of detection: <120 ng/mL

KEY WORDS

whole blood; plasma; interferences may occur—compounds(all of which are extracted) elute in this order tenoxicam; iproniazid; methocarbamol; methotrexate; caffeine; nialamide; colchicine; cytarabine; benzoylecgonine; acetaminophen; diazoxide; dacarbazine; sulfinpyrazole; flumazenil; sulpride; morphine; atenolol; toloxatone; terbutaline; albuterol; phenobarbital; ranitidine; tiapride; phenol; chlormezanone; aspirin; metformin; ritodrine; codeine; sultopride; amisulpride; naltrexone; lisinopril; benzocaine; nizatidine; nalorphine; mephenesin; naloxone; sotalol; carteolol; procainamide; carbamazepine; bromazepam; nalbuphine; nadolol; procarbazine; dihydralazine; omeprazole; strychnine; acebutolol; glutethimide; chlorpropamide; glipizide; triazolam; prazosin; flunitrazepam; clonazepam; metoclopramide; melphalan; estazolam; tolbutamide; ephedrine; clonidine; pindolol; clobazam; minoxidil; disopyramide; nitrazepam; dextromethorphan; tofisopam; zopiclone; debrisoquine; sulindac; alprazolam; cycloguanil; lorazepam; methaqualone; ketamine; piroxicam; metoprolol; nifedipine; quinine; mephentermine; prilocaine; pentazocine; oxazepam; tiaprofenic acid; quinidine; celiprolol; ajmaline; yohimbine; lidocaine; secobarbital; viloxazine; mepivacaine; meperidine; doxylamine; labetalol; temazepam; amodiaquine; benperidol; droperidol; hydroxychloroquine; zolpidem; ketoprofen; alminoprofen; cicletanine; moclobemide; chloroquine; cocaine; timolol; nomifensine; ticlopidine; acenocoumarol; videsine; mexiletine; dipyridamole; trazodone; pipamperone; pyrimethamine; benazepril; vincristine; metapramine; chlordiazepoxide; oxprenolol; warfarin; clorazepate; flecainide; phenacyclidine; thiopental; fenfluramine; metipranolol; triprolidine; naproxen; buprenorphine; verapamil; buspirone; tianeptine; midazolam; bupivacaine; carbinoxamine; loperazolam; cetirizine; chlorpheniramine; moperone; cibenzoline; medifoxamine; astemizole; vinblastine; nicardipine; bisoprolol; diltiazem; glibornuride; reserpine;

aconitine; nitrendipine; diazepam; mianserin; ramipril; haloperidol; tetracaine; alprenolol; aceprometazine; glibenclamide; chlorophenacinone; doxepin; nimodipine; diphenhydramine; cyclizine; histapyrrodine; phenylbutazone; demoxiptiline; clozapine; proguanil; trifluoperidol; medazepam; cyamemazine; bumadizone; suriclone; propranolol; acepromazine; dothiepin; dextromoramide; fenpropfen; dextropropoxyphene; loxapine; betaxolol; propafenone; promethazine; thiopropazine; methadone; amoxapine; quinupramine; opipramol; cyproheptadine; brompheniramine; mefenidramine; protriptyline; flurbiprofen; tetrazepam; zorubicin; prazepam; alimemazine; loperamide; imipramine; desipramine; levomepromazine; hydroxyzine; niflumic acid; penbutolol; fluvoxamine; pimozone; daunorubicin; indomethacin; maprotiline; tropatenine; etodolac; fluoxetine; amitriptyline; nortriptyline; tiocloamarol; diclofenac; mefloquine; trimipramine; chlorambucil; lidoflazine; ibuprofen; floctafenine; alpidem; loratadine; chlorpromazine; clomipramine; carpipramine; thioridazine; fentiazac; clemastine; mefenamic acid; fluphenazine; prochlorperazine; penfluridol; bepridil; terfenadine; trifluoperazine

REFERENCE

Tracqui,A.; Kintz,P.; Mangin,P. Systematic toxicological analysis using HPLC/DAD, *J.Forensic Sci.*, **1995**, *40*, 254–262.

SAMPLE

Matrix: blood, CSF

Sample preparation: Plasma. Centrifuge blood at 7000 rpm, decant 100 μ L plasma. Mix 100 μ L plasma with 200 μ L acetone, centrifuge at 7000 rpm for 5 min. Evaporate the supernatant under a stream of nitrogen, reconstitute the residue with mobile phase, inject an aliquot. CSF. Add 25 μ L water to 25 μ L CSF, mix with 50 μ L acetone, centrifuge at 7000 rpm for 5 min, decant the supernatant, evaporate under a stream of nitrogen, reconstitute the residue with mobile phase, inject an aliquot.

HPLC VARIABLES

Column: μ Bondapak C18

Mobile phase: MeOH:water 58.5:41.5 containing 20 mM butylamine

Column temperature: 60

KEY WORDS

plasma; rat; pharmacokinetics

REFERENCE

Chou,K.-J.; Donovan,M.D. Distribution of antihistamines into the CSF following intranasal delivery, *Biopharm.Drug Dispos.*, **1997**, *18*, 335–346.

SAMPLE

Matrix: blood, tissue

Sample preparation: Blood or serum. 1 mL Blood or serum + 1 μ g cianopramine + 1 mL water, vortex, add 1 mL 200 mM sodium carbonate, vortex, add 6 mL hexane:1-butanol 95:5, gently agitate for 30 min, centrifuge at 2500 g for 5 min. Remove the organic layer and add it to 100 μ L 0.2% phosphoric acid, agitate gently for 30 min, centrifuge for 5 min. Remove the organic layer and inject a 30 μ L aliquot of the aqueous layer. Liver homogenate. 0.5 mL Liver homogenate + 10 μ g cianopramine + 500 μ L 2% sodium tetraborate + 8 mL hexane:1-butanol 95:5, gently agitate for 30 min, centrifuge at 2500 g for 5 min. Remove the organic layer and add it to 400 μ L 0.2% phosphoric acid, agitate gently for 30 min, centrifuge for 5 min. Remove the organic layer and inject a 30 μ L aliquot of the aqueous layer.

HPLC VARIABLES

Guard column: 15 \times 3.2 7 μ m RP-18 Newguard (Applied Biosystems)

Column: 100 \times 4.6 5 μ m Brownlee Spheri-5 RP-18

Mobile phase: MeCN:100 mM NaH₂PO₄:diethylamine 40:57.5:2.5

Flow rate: 2
Injection volume: 30
Detector: UV 220

CHROMATOGRAM

Retention time: 8.86
Internal standard: cianopramine (8.93)

OTHER SUBSTANCES

Simultaneous: amitriptyline, amoxapine, benzotropine, brompheniramine, chlorpromazine, clomipramine, cyproheptadine, desipramine, diphenhydramine, dothiepin, doxepin, fluoxetine, haloperidol, imipramine, loxapine, maprotiline, meperidine, mesoridazine, methadone, metoclopramide, mianserin, moclobemide, nomifensine, nordoxepin, norfluoxetine, norpropoxyphene, nortriaden, nortriptyline, pentobarbital, pheniramine, promethazine, propoxyphene, propranolol, protriptyline, quinidine, quinine, sulforidazine, thioridazine, thiothixene, tranilcypramine, trazodone, trihexyphenidyl, trimipramine, triprolidine
Noninterfering: dextromethorphan, norphethidine, phenoxybenzamine, prochlorperazine, trifluoperazine

KEY WORDS

serum; whole blood; liver

REFERENCE

McIntyre, I.M.; King, C.V.; Skafidis, S.; Drummer, O.H. Dual ultraviolet wavelength high-performance liquid chromatographic method for the forensic or clinical analysis of seventeen antidepressants and some selected metabolites, *J.Chromatogr.*, **1993**, 621, 215–223.

SAMPLE

Matrix: blood, urine

Sample preparation: 500 μ L Serum or urine + 100 μ L 2 M NaOH + 2.5 mL chloroform: isopropanol 95:5, shake vigorously for 20 min, centrifuge at 700 g for 5 min. Remove the organic layer and add it to 100 μ L 50 mM sulfuric acid, mix vigorously on a shaker for 10 min, inject a 20 μ L aliquot of the aqueous layer.

HPLC VARIABLES

Column: 300 \times 3.9 10 μ m μ Bondapak C18
Mobile phase: MeOH:water 70:30 containing 5 mM sodium heptanesulfonate
Flow rate: 1.2
Injection volume: 20
Detector: UV 260

CHROMATOGRAM

Retention time: 4.9
Internal standard: chlorpheniramine

OTHER SUBSTANCES

Simultaneous: chlorhexidine, p-chloroaniline
Noninterfering: benzyl alcohol, benzoic acid, phosphanilic acid

KEY WORDS

serum; chlorpheniramine is IS

REFERENCE

Brougham, L.R.; Cheng, H.; Pittman, K.A. Sensitive high-performance liquid chromatographic method for the determination of chlorhexidine in human serum and urine, *J.Chromatogr.*, **1986**, 383, 365–373.

SAMPLE

Matrix: blood, urine

Sample preparation: Add 1 mL whole blood or urine to Toxi-Tube A (Toxi-Lab, Irvine CA), add 3 mL water, mix by gentle inversion for 5 min, centrifuge at 1500 g for 5 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen at 40°, reconstitute the residue with 50 µL MeCN:water 50:50, vortex for 10 s, centrifuge at 7500 g for 2 min, inject a 10 (urine) or 30 (blood) µL aliquot. (The detector wavelength shown is the wavelength of maximum absorbance. This will not necessarily be the optimal wavelength for the separation. Multiple wavelengths from 200-350 nm can be scanned using a diode-array detector. Otherwise, 220 nm may be a reasonable choice for initial work. Matrix may interfere.)

HPLC VARIABLES

Guard column: 20 mm long Symmetry C18

Column: 250 × 4.6 5 µm Symmetry C8 (Waters)

Mobile phase: Gradient. A was 50 mM pH 3.8 sodium phosphate buffer. B was MeCN. A: B 85:15 for 6.5 min, 65:35 for 18.5 min, 20:80 for 3 min (step gradient), re-equilibrate at initial conditions for 7 min.

Column temperature: 30

Flow rate: 1 for 6.5 min, to 1.5 over 18.5 min, maintain at 1.5 for 3 min (re-equilibrate at 1.5 mL/min)

Injection volume: 10-30

Detector: UV 200.5

CHROMATOGRAM

Retention time: 12.925

KEY WORDS

whole blood

REFERENCE

Gaillard, Y.; Pépin, G. Use of high-performance liquid chromatography with photodiode-array UV detection for the creation of a 600-compound library. Application to forensic toxicology, *J.Chromatogr.A*, **1997**, 763, 149-163.

SAMPLE

Matrix: cell incubations

Sample preparation: 40 mL Cell incubation + 50 mL MeOH, shake vigorously for 1 min, centrifuge at 2000 rpm for 10 min, wash the pellet twice with 50 mL portions of MeOH. Combine the supernatants and add 100 mL water, extract three times with 150 mL portions of dichloromethane. Filter the extracts through anhydrous sodium sulfate, evaporate the filtrate to dryness under reduced pressure at 40°, reconstitute with mobile phase, inject an aliquot.

HPLC VARIABLES

Column: 250 × 4.6 5 µm cyano-propyl (Beckman)

Mobile phase: MeCN:buffer 40:60 (Buffer was 10 mM KH₂PO₄ containing 20 mM triethylamine, pH 7.0.)

Flow rate: 1

Injection volume: 20

Detector: UV 254

CHROMATOGRAM

Retention time: 9.4

OTHER SUBSTANCES

Extracted: metabolites

Interfering: brompheniramine, pheniramine

KEY WORDS

also semipreparative details

REFERENCE

Hansen, E.B., Jr.; Cho, B.P.; Korfmacher, W.A.; Cerniglia, C.E. Fungal transformations of antihistamines: metabolism of brompheniramine, chlorpheniramine, and pheniramine to *N*-oxide and *N*-demethylated metabolites by the fungus *Cunninghamella elegans*, *Xenobiotica*, **1995**, 25, 1081–1092.

SAMPLE

Matrix: formulations

HPLC VARIABLES

Column: 150 × 6 5 μm Capcell Pak C8 (Shiseido, Japan)

Mobile phase: MeOH:50 mM KH₂PO₄ containing 5 mM tetra-*n*-butylammonium phosphate 15:85, adjusted to pH 2.6 with 5% orthophosphoric acid (After one week of use, wash the column with water and MeOH:water 70:30 at 1 mL/min for 30 min.)

Column temperature: 30

Flow rate: 1

Injection volume: 10–20

Detector: UV 215

CHROMATOGRAM

Retention time: 7.45

OTHER SUBSTANCES

Simultaneous: dipotassium glycyrrizate, fumaric acid, *m*-hydroxybenzoic acid, *p*-hydroxybenzoic acid, maleic acid, neostigmine methylsulfate, pyridoxine, tetrahydrozoline, vitamin B12

Noninterfering: chondroitin sulfate, lysozyme

KEY WORDS

ophthalmic solutions; ion-pair agents

REFERENCE

Yamato, S.; Nakajima, M.; Shimada, K. Simultaneous determination of chlorpheniramine and maleate by high-performance liquid chromatography using tetra-*n*-butylammonium phosphate as an ion-pair reagent, *J.Chromatogr.A*, **1996**, 731, 346–350.

SAMPLE

Matrix: formulations

Sample preparation: Grind tablets to a powder, completely dissolve in 100 mL water, vortex mechanically for 5 min, centrifuge an aliquot at 3000 rpm for 5 min. Remove a 300 μL aliquot of the supernatant, add 20 μL 100 μg/mL IS in MeOH, dilute to 1 mL with MeCN, inject a 20 μL aliquot.

HPLC VARIABLES

Column: 100 × 8 10 μm μBondapak C18

Mobile phase: MeCN:buffer 60:40 (Buffer was 50 mM ammonium acetate adjusted to pH 3.5 with glacial acetic acid.)

Flow rate: 1.8

Injection volume: 20

Detector: UV 265

CHROMATOGRAM

Retention time: 5.42

Internal standard: propylparaben (8.45)

Limit of quantitation: 500 ng/mL

KEY WORDS

tablets

REFERENCE

Al-Deeb, O.A.; Foda, N.H.; El Shafie, F.; Al-Affi, A. High performance liquid chromatographic assay of chlorpheniramine maleate in tablet formulations, *J.Liq.Chromatogr.Rel.Technol.*, **1997**, *20*, 2221–2231.

SAMPLE

Matrix: formulations

Sample preparation: Tablets. Powder tablets, weigh out amount equivalent to about 10 mg, add 75 mL mobile phase, sonicate for 20 min, dilute to 100 mL with mobile phase, mix, filter (0.45 μ m) (discard first 10 mL of filtrate), inject a 20 μ L aliquot of the filtrate. Syrups, elixirs, injectables. Measure out amount equivalent to about 10 mg, add 75 mL mobile phase, sonicate for 20 min, dilute to 100 mL with mobile phase, mix, inject a 20 μ L aliquot.

HPLC VARIABLES

Column: 300 \times 3.9 10 μ m μ Bondapak CN

Mobile phase: MeOH:3 mM ammonium acetate 90:10

Flow rate: 1.3

Injection volume: 20

Detector: UV 254

CHROMATOGRAM

Retention time: 4.3

OTHER SUBSTANCES

Also analyzed: cyclizine, doxylamine, mesoridazine, pentazocine, promethazine, protriptyline, pyrilamine, pyrimethamine, tripeleennamine

KEY WORDS

tablets; syrups; elixirs; injections

REFERENCE

Walker, S.T. Liquid chromatographic determination of organic nitrogenous bases in dosage forms: a progress report, *J.Assoc.Off.Anal.Chem.*, **1985**, *68*, 539–542.

SAMPLE

Matrix: formulations

Sample preparation: Grind tablet, dissolve in 100 mL 100 mM pH 5.0 acetate buffer, let sit for 1 h with occasional mixing, filter (0.45 μ m), inject a 50 μ L aliquot.

HPLC VARIABLES

Column: 250 \times 4.6 Zorbax SCX

Mobile phase: MeCN:30 mM KH_2PO_4 50:50

Flow rate: 2

Injection volume: 50

Detector: UV 263

CHROMATOGRAM

Retention time: 16.0

OTHER SUBSTANCES

Simultaneous: pseudoephedrine, dextromethorphan

KEY WORDS

tablets

REFERENCE

Murtha,J.L.; Julian,T.N.; Radebaugh,G.W. Simultaneous determination of pseudoephedrine hydrochloride, chlorpheniramine maleate, and dextromethorphan hydrobromide by second-derivative photodiode array spectroscopy, *J.Pharm.Sci.*, **1988**, 77, 715-718.

SAMPLE

Matrix: formulations

Sample preparation: Crush tablets, add 100 mL water and 30-40 mL MeCN, dissolve, add N,N-dimethylbenzylamine, make up to 250 or 500 mL with water, centrifuge an aliquot, inject a 20 μ L aliquot of the supernatant.

HPLC VARIABLES

Column: 150 \times 4.6 Asahipak ODP-50 C18

Mobile phase: MeCN:200 mM pH 7.0 phosphate buffer 27:73

Flow rate: 0.8

Injection volume: 20-100

Detector: Chemiluminescence following post-column reaction. Oxidize a 1 mM tris(2,2'-bipyridine) ruthenium(II) hexachloride solution in 50 mM pH 5.5 acetate buffer to Ru(III) using a Princeton Applied Research polarographic analyzer with a platinum gauze working electrode, platinum wire auxiliary electrode, and a silver wire reference electrode, +950 mV. Pump the reagent solution at 0.28 mL/min and mix with the column effluent, allow to flow through detector. The chemiluminescence detector was a fluorescence detector with the light source removed.

CHROMATOGRAM

Retention time: 7

Internal standard: N,N-dimethylbenzylamine

Limit of detection: 140 ng/mL

OTHER SUBSTANCES

Simultaneous: brompheniramine, diphenhydramine, pyrilamine, pheniramine

KEY WORDS

tablets

REFERENCE

Holeman,J.A.; Danielson,N.D. Liquid chromatography of antihistamines using post-column tris(2,2'-bipyridine) ruthenium(III) chemiluminescence detection, *J.Chromatogr.A*, **1994**, 679, 277-284.

SAMPLE

Matrix: formulations

Sample preparation: Finely powder half a tablet, add 9 mL mobile phase, sonicate for 20 min, make up to 10 mL with mobile phase, filter (Whatman type 40 and 0.2 μ m Millipore), inject an aliquot of the filtrate.

HPLC VARIABLES

Column: 250 \times 4.5 μ m LiChrospher 100 CN

Mobile phase: MeCN:THF:buffer 7:6:87 (Buffer was 0.8% acetic acid containing 5 mM sodium hexanesulfonate, 10 mM di-n-butylamine, and 0.12% phosphoric acid, pH 3.3.)

Flow rate: 1

Injection volume: 20

Detector: UV 265

CHROMATOGRAM

Retention time: 7.8

Limit of detection: 2.9 µg/mL

OTHER SUBSTANCES

Simultaneous: acetaminophen (UV 310), caffeine (UV 298), guaifenesin (glycerylguaiacolate) (UV 284), phenylpropanolamine (UV 260)

KEY WORDS

tablets

REFERENCE

Indrayanto,G.; Sunarto,A.; Adriani,Y. Simultaneous assay of phenylpropanolamine hydrochloride, caffeine, paracetamol, glycerylguaiacolate and chlorpheniramine in Silabat™ tablet using HPLC with diode array detection, *J.Pharm.Biomed.Anal.*, **1995**, 13, 1555–1559.

SAMPLE

Matrix: formulations

Sample preparation: Dilute syrup with mobile phase to a concentration of 5-100 µg/mL, shake, filter, inject an aliquot.

HPLC VARIABLES

Column: 250 × 4.6 5 µm 80 Å Ultrasphere CN

Mobile phase: MeCN:water:EtOH 60:38:2 containing 1 mM perchloric acid

Column temperature: 30

Flow rate: 1

Injection volume: 20

Detector: Conductivity, zero suppression 2, range 1 or 10

CHROMATOGRAM

Retention time: 21.2

OTHER SUBSTANCES

Simultaneous: bromhexine, codeine, dextromethorphan, diphenhydramine, ephedrine, papaverine, phenylephrine

KEY WORDS

syrup; indirect conductometric detection; presence of compound causes a decrease in mobile phase conductivity

REFERENCE

Lau,O.-W.; Mok,C.-S. High-performance liquid chromatographic determination of active ingredients in cough-cold syrups with indirect conductometric detection, *J.Chromatogr.A*, **1995**, 693, 45–54.

SAMPLE

Matrix: formulations

Sample preparation: Condition a 500 mg Bond Elut SCX strong cation-exchange SPE cartridge with 6 mL MeOH and 3 mL 10 mM pH 4.5 phosphate buffer. Weigh out powdered tablet containing 0.45 mg chlorpheniramine, add 25 mL MeCN:10 mM pH 4.5 phosphate buffer 25:75, sonicate for 10 min, dilute to 50 mL with 10 mM pH 4.5 phosphate buffer, centrifuge, add a 10 mL aliquot of the supernatant to the SPE cartridge, wash with four 3 mL portions of 10 mM pH 4.5 phosphate buffer, elute with 4 mL MeCN:100 mM pH 8.0 triethylamine phosphate 40:60, inject an aliquot.

HPLC VARIABLES

Column: 150 × 4.6 5 µm Spherisorb CN

Mobile phase: MeCN:100 mM pH 3.0 triethylamine phosphate 5:95

Flow rate: 1

Injection volume: 20

Detector: UV 275 or UV 330 following post-column reaction. The column effluent flowed through a 10 m \times 0.3 mm ID crocheted PTFE coil irradiated with an 8 W low-pressure mercury lamp at 254 nm to the detector.

CHROMATOGRAM

Retention time: 4.7

OTHER SUBSTANCES

Noninterfering: acetaminophen, caffeine

KEY WORDS

post-column reaction; post-column photochemical derivatization; SPE; tablets

REFERENCE

Di Pietra,A.M.; Gatti,R.; Andrisano,V.; Cavrini,V. Application of high-performance liquid chromatography with diode-array detection and on-line post-column photochemical derivatization to the determination of analgesics, *J.Chromatogr.A*, **1996**, 729, 355–361.

SAMPLE

Matrix: incubations

Sample preparation: Extract incubation mixture with four volumes of cold dichloromethane for 3 min, centrifuge at 1000 g for 5 min. Remove the organic layer and pass it through a nylon filter, evaporate the filtrate to dryness, reconstitute the residue in 500 μ L MeOH, inject a 15 μ L aliquot.

HPLC VARIABLES

Column: 250 \times 4.5 5 μ m AXXIOM silica (Richard Scientific)

Mobile phase: MeCN:MeOH:60% aqueous perchloric acid 60:40:0.08

Flow rate: 1

Injection volume: 15

Detector: UV 260

CHROMATOGRAM

Retention time: 6.5

Limit of detection: 5-20 ng/mL

OTHER SUBSTANCES

Extracted: brompheniramine N-oxide, chlorpheniramine N-oxide

Interfering: brompheniramine

KEY WORDS

ion-pair; desorption; chromatography; incubations

REFERENCE

Cashman,J.R.; Yang,Z.-C. Analysis of amine metabolites by high-performance liquid chromatography on silica gel with a non-aqueous ionic eluent, *J.Chromatogr.*, **1990**, 532, 405–410.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 \times 4 ODS (Hitachi)

Mobile phase: MeCN:50 mM phosphoric acid 40:60 containing 400 mM KCl

Column temperature: 55

Flow rate: 0.6

Injection volume: 20

Detector: UV 265

OTHER SUBSTANCES

Also analyzed: antipyrine

REFERENCE

Sugawara, M.; Takekuma, Y.; Yamada, H.; Kobayashi, M.; Iseki, K.; Miyazaki, K. A general approach for the prediction of the intestinal absorption of drugs: regression analysis using the physicochemical properties and drug-membrane electrostatic interactions, *J. Pharm. Sci.*, **1998**, 87, 960–966.

SAMPLE

Matrix: solutions

Sample preparation: Prepare a 10 µg/mL solution in MeOH, inject a 20 µL aliquot.

HPLC VARIABLES

Column: 125 × 4.9 Spherisorb S5W silica

Mobile phase: MeOH containing 10 mM ammonium perchlorate and 1 mL/L 100 mM NaOH in MeOH, pH 6.7

Flow rate: 2

Injection volume: 20

Detector: E, LeCarbone, V25 glassy carbon electrode, + 1.2 V

CHROMATOGRAM

Retention time: 4.2

OTHER SUBSTANCES

Also analyzed: acebutolol, acepromazine, acetophenazine, N-acetylprocainamide, albuterol, alprenolol, amethocaine, amiodarone, amitriptyline, antazoline, atenolol, azacyclonal, bamethan, benactyzine, benperidol, benzethidine, benzocaine, benzocetamine, benzphetamine, benzquinamide, bromhexine, bromodiphenhydramine, bromperidol, brompheniramine, brompromazine, buclizine, bufotenine, bupivacaine, buprenorphine, butacaine, butethamate, chlorcyclizine, chlorphenoxamine, chlorprenaline, chlorpromazine, chlorprothixene, cimetidine, cinchonidine, cinnarizine, clemastine, clomipramine, clonidine, cocaine, cyclazocine, cyclizine, cyclopentamine, cyproheptadine, deserpidine, desipramine, dextromoramide, dextropropoxyphene, dicyclomine, diethylcarbamazepine, diethylpropion, diethylthiambutene, dihydroergotamine, dimethindene, dimethothiazine, diphenhydramine, diphenoxylate, dipipanone, diprenorphine, dipyrizamide, disopyramide, dothiepin, doxapram, doxepin, doxylamine, droperidol, ephedrine, ergocornine, ergocristine, ergocristinine, ergocryptine, ergometrine, ergosine, ergosinine, ergotamine, ethopropazine, etorphine, etoxeridine, fenethazine, fenfluramine, fenoterol, fentanyl, flavoxate, fluopromazine, flupenthixol, fluphenazine, flurazepam, haloperidol, hydroxyzine, hyoscine, ibogaine, imipramine, indapamine, iprindole, isothipendyl, isoxsuprine, ketanserine, laudanosine, lidocaine, lofepramine, loxapine, maprotiline, mecamlamine, meclophenoxate, meclozine, medazepam, mephentermine, mepivacaine, meptazinol, mepyramine, mesoridazine, metaraminol, methadone, methamphetamine, methapyrilene, methdilazene, methotrimeprazine, methoxamine, methoxyphenamine, methoxypropazine, methylephedrine, methylergonovine, methysergide, metoclopramide, metopimazine, metoprolol, mianserin, morazone, nadolol, nalorphine, naloxone, naphazoline, nicotine, nifedipine, nomifensine, nortriptyline, noscapine, orphenadrine, oxeladin, oxprenolol, oxymetazolin, papaverine, pargyline, pecazine, penbutolol, pentazocine, penthienate, pericyazine, perphenazine, phenadoxone, phenampromide, phenazocine, phenbutrazate, phendimetrazine, phenelzine, phenglutarimide, phenindamine, pheniramine, phenmetrazine, phenomorphan, phenoperidine, phenothiazine, phenoxybenzamine, phentolamine, phenylephrine, phenyltoloxamine, physostigmine, piminodine, pimozone, pindolol, pipamazine, pipazethate, piperacetazine, piperidolate, pipradol, pirenzepine, piritramide, pizotifen, practolol, pramoxine, prazosin, prenylamine, prilocaine, primaquine, proadifen, procainamide, procaine, prochlorperazine, procyclidine, proheptazine, prolintane, promazine, promethazine, pronethalol, properidine, propiomazine, propranolol, prothipendyl, protriptyline, proxymetacaine, pseudoephedrine, pyrimethamine, quinidine, quinine, ranitidine, rescinnamine, sotalol, tacrine, terazosin, terbutaline, terfenadine, thenyldiamine,

theophylline, thiethylperazine, thiopropazate, thioproperazine, thioridazine, thiothixene, thonzylamine, timolol, tocanide, tolpropamine, tolycaine, tranylcypromine, trazodone, tri-fluoperazine, trifluoperidol, trimeperidine, trimeprazine, trimethobenzamide, trimetho-prim, trimipramine, tripeleennamine, triprolidine, tryptamine, verapamil, xylometazoline

REFERENCE

Jane,I.; McKinnon,A.; Flanagan,R.J. High-performance liquid chromatographic analysis of basic drugs on silica columns using non-aqueous ionic eluents. II. Application of UV, fluorescence and electro-chemical oxidation detection, *J.Chromatogr.*, **1985**, 323, 191–225.

SAMPLE

Matrix: solutions

Sample preparation: Dissolve in MeOH:water 1:1 at a concentration of 50 µg/mL, inject a 10 µL aliquot.

HPLC VARIABLES

Column: 300 × 3.9 10 µm µBondapak C18

Mobile phase: MeOH:acetic acid:triethylamine:water 50:1.5:0.5:48

Flow rate: 1.5

Injection volume: 10

Detector: UV 254

CHROMATOGRAM

Retention time: 7

OTHER SUBSTANCES

Simultaneous: thonzylamine, pheniramine, tripeleennamine, brompheniramine, pheninda-mine, phenyltoxamine, clemizole

REFERENCE

Roos,R.W.; Lau-Cam,C.A. General reversed-phase high-performance liquid chromatographic method for the separation of drugs using triethylamine as a competing base, *J.Chromatogr.*, **1986**, 370, 403–418.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4.6 cellulose tris(3,5-dimethylphenylcarbamate)

Mobile phase: Hexane:isopropanol 98:2

Flow rate: 0.5

Detector: UV

CHROMATOGRAM

Retention time: k' 1.75 (of first (-) enantiomer)

KEY WORDS

chiral; α 1.09

REFERENCE

Okamoto,Y.; Aburatani,R.; Hatano,K.; Hatada,K. Optical resolution of racemic drugs by chiral HPLC on cellulose and amylose tris(phenylcarbamate) derivatives, *J.Liq.Chromatogr.*, **1988**, 11, 2147–2163.

SAMPLE

Matrix: solutions

Sample preparation: Prepare a 7.6 µg/mL solution, inject a 10 µL aliquot.

HPLC VARIABLES**Guard column:** Supelguard LC-8-DB (Supelco)**Column:** 50 × 4.6 Supelcosil LC-8-DB**Mobile phase:** MeCN:buffer 10:90 containing 0.02% triethylamine (Buffer was KH_2PO_4 adjusted to pH 2.0 with phosphoric acid.)**Column temperature:** 35**Flow rate:** 2**Injection volume:** 10**Detector:** UV 254

CHROMATOGRAM**Retention time:** 3.5

OTHER SUBSTANCES**Simultaneous:** methscopolamine, phenylpropanolamine, pseudoephedrine, triprolidine

REFERENCE*Supelco Catalog, 1992, p. 179.*

SAMPLE**Matrix:** solutions

HPLC VARIABLES**Guard column:** Supelguard (Supelco)**Column:** 150 × 4.6 5 μm Supelcosil LC-8-DB**Mobile phase:** MeCN:MeOH:buffer 19:28:53 (Buffer was 50 mM KH_2PO_4 containing 0.2% triethylamine, pH 2.5.)**Flow rate:** 1.5**Injection volume:** 10**Detector:** UV 254

CHROMATOGRAM**Retention time:** 2.5

OTHER SUBSTANCES**Simultaneous:** chlorcyclizine, clonidine, diphenhydramine, promethazine, pyrilamine, triprolidine

REFERENCE*Supelco Catalog, 1994, 768.*

SAMPLE**Matrix:** solutions

HPLC VARIABLES**Column:** 250 × 4.6 Zorbax RX**Mobile phase:** Gradient. A was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 1 L water. B was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 200 mL water, make up to 1 L with MeCN. A:B from 100:0 to 0:100 over 30 min, maintain at 0:100 for 5 min.**Column temperature:** 30**Flow rate:** 2**Detector:** UV 210

OTHER SUBSTANCES**Also analyzed:** acepromazine, acetaminophen, acetophenazine, albuterol, aminophylline, amitriptyline, amobarbital, amoxapine, amphetamine, amylocaine, antipyrine, aprobarbital, aspirin, atenolol, atropine, avermectin, barbital, benzocaine, benzoic acid, benzotro-

pine, benzphetamine, berberine, bibucaine, bromazepam, brompheniramine, buprenorphine, buspirone, butabarbital, butacaine, butethal, caffeine, carbamazepine, carbromal, chloramphenicol, chlordiazepoxide, chloroquine, chlorothiazide, chloroxylenol, chlorpromazine, chlorpropamide, chlortetracycline, cimetidine, cinchonidine, cinchonine, clenbuterol, clonazepam, clonixin, clorazepate, cocaine, codeine, colchicine, cortisone, coumarin, cyclazocine, cyclobenzaprine, cyclothiazide, cyheptamide, cymarin, danazol, danthron, dapson, debrisoquine, desipramine, dexamethasone, dextromethorphan, dextropropoxyphene, diamorphine, diazepam, diclofenac, diethylpropion, diethylstilbestrol, diflunisal, digitoxin, digoxin, diltiazem, diphenhydramine, diphenoxylate, diprenorphine, dipyrone, disulfiram, dopamine, doxapram, doxepin, dronabinol, ephedrine, epinephrine, epinine, estradiol, estriol, estrone, ethacrynic acid, ethosuximide, etonitazene, etorphine, eugenol, famotidine, fenbendazole, fencamfamine, fenoprofen, fenproporex, fentanyl, flubendazole, flufenamic acid, flunitrazepam, 5-fluorouracil, fluoxymesterone, fluphenazine, furosemide, gentisic acid, gitoxigenin, glipizide, glunixin, glutethimide, glybenclamide, guaiacol, halazepam, haloperidol, hydrochlorothiazide, hydrocodone, hydrocortisone, hydromorphone, hydroxyquinoline, ibogaine, ibuprofen, iminostilbene, imipramine, indomethacin, isocarboxtyril, isocarboxazid, isoniazid, isoproterenol, isoxsuprine, ivermectin, ketamine, ketoprofen, kynurenic acid, levorphanol, lidocaine, lorazepam, lormetazepam, loxapine, mazindol, mebendazole, meclizine, meclofenamic acid, medazepam, mefenamic acid, megestrol, mepacrine, meperidine, mephentermine, mephenytoin, mephesin, mephobarbital, mepivacaine, mescaline, mesoridazine, methadone, methamphetamine, methapyrilene, methaqualone, methazolamide, methocarbamol, methoxamine, methsuximide, methyl salicylate, methyl dopa, methyl dopamine, methylphenidate, methylprednisolone, methyltestosterone, methyprylon, metoprolol, mibolerone, morphine, nadolol, nalorphine, naloxone, naltrexone, naphazoline, naproxen, nefopam, niacinamide, nicotine, niacin, nifedipine, niflumic acid, nitrazepam, norepinephrine, nortriptyline, noscapine, nyldrin, oxazepam, oxycodone, oxymorphone, oxyphenbutazone, oxytetracycline, papaverine, pargyline, pemoline, pentazocine, pentobarbital, persantine, phenacetin, phenazocine, phenazopyridine, phencyclidine, phendimetrazine, phenelzine, pheniramine, phenobarbital, phenothiazine, phensuximide, phentermine, phenylbutazone, phenylephrine, phenylpropanolamine, piperocaine, prazepam, prednisolone, primidone, probenecid, progesterone, propiomazine, propranolol, propylparaben, pseudoephedrine, puromycin, pyrilamine, pyrithyldione, quazepam, quinaldic acid, quinidine, quinine, ranitidine, recinnamine, reserpine, resorcinol, saccharin, albuterol, salicylamide, salicylic acid, scopolamine, scopoletin, secobarbital, strychnine, sulfacetamide, sufadiazine, sulfadimethoxine, sulfaethidole, sulfamerazine, sulfamethazine, sulfamethoxazole, sulfanilamide, sulfapyridine, sulfasoxazole, sulindac, tamoxifen, temazepam, testosterone, tetracaine, tetracycline, tetramisole, thebaine, theobromine, theophylline, thiabendazole, thiamine, thiamylal, thiobarbituric acid, thioridazine, thiosalicylic acid, thiothixene, thymol, tolazamide, tolazoline, tobutamide, tolmetin, tranlycypromine, triamcinolone, tribenzylamine, trichloromethiazide, trifluoperazine, trihexyphenidyl, trimethoprim, tripeleppamine, triprolidine, tropacocaine, tyramine, verapamil, vincamine, warfarin, yohimbine, zoxazolamine

REFERENCE

Hill,D.W.; Kind,A.J. Reversed-phase solvent gradient HPLC retention indexes of drugs, *J.Anal.Toxicol.*, **1994**, *18*, 233–242.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 150 × 4.6 12 μ m 1-myristoyl-2-[(13-carboxyl)-tridecoyl]-sn-3-glycerophosphocholine chemically bonded to silica (Regis)

Mobile phase: MeCN:100 mM pH 7.0 phosphate buffer 20:80

Flow rate: 1

Detector: UV 254

CHROMATOGRAM

Retention time: k' 11.35

OTHER SUBSTANCES

Also analyzed: acebutolol, alprenolol, antazoline, atenolol, betaxolol, bisoprolol, bopindolol, bupranolol, carteolol, celiprolol, chloropyramine, cicloprolol, cimetidine, cinnarizine, cirazoline, clonidine, dilevalol, dimethindene, diphenhydramine, doxazosin, esmolol, famotidine, isothipendyl, ketotifen, metiamide, metoprolol, moxonidine, nadolol, naphazoline, nifenalol, nizatidine, oxprenolol, pheniramine, phentolamine, pindolol, pizotyline (pizotifen), practolol, prazosin, promethazine, propranolol, pyrilamine (mepyramine), ranitidine, roxatidine, sotalol, tiamenidine, timolol, tramazoline, tripeleppamine, triprolidine, tymazoline, UK-14,304

REFERENCE

Kaliszan, R.; Nasal, A.; Turowski, M. Binding site for basic drugs on α_1 -acid glycoprotein as revealed by chemometric analysis of biochromatographic data, *Biomed. Chromatogr.*, **1995**, 9, 211–215.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4.6 5 μ m Supelcosil LC-DP (A) or 250 × 4.5 μ m LiChrospher 100 RP-8 (B)

Mobile phase: MeCN:0.025% phosphoric acid:buffer 25:10:5 (A) or 60:25:15 (B) (Buffer was 9 mL concentrated phosphoric acid and 10 mL triethylamine in 900 mL water, adjust pH to 3.4 with dilute phosphoric acid, make up to 1 L.)

Flow rate: 0.6

Injection volume: 25

Detector: UV 229

CHROMATOGRAM

Retention time: 10.80 (A), 5.25 (B)

OTHER SUBSTANCES

Also analyzed: acebutolol, acepromazine, acetaminophen, acetazolamide, acetophenazine, albuterol, alprazolam, amitriptyline, amobarbital, amoxapine, antipyrine, atenolol, atropine, azatadine, baclofen, benzocaine, bromocriptine, brompheniramine, brotizolam, bupivacaine, buspirone, butabarbital, butalbital, caffeine, carbamazepine, cetirizine, chlorcyclizine, chlordiazepoxide, chlormezanone, chloroquine, chlorpromazine, chlorpropamide, chlorprothixene, chlorthalidone, chlorzoxazone, cimetidine, cisapride, clomipramine, clonazepam, clonidine, clozapine, cocaine, codeine, colchicine, cyclizine, cyclobenzaprine, dantrolene, desipramine, diazepam, diclofenac, diflunisal, diltiazem, diphenhydramine, diphenidol, diphenoxylate, dipyrindamole, disopyramide, dobutamine, doxapram, doxepin, droperidol, encainide, ethidium bromide, ethopropazine, fenoprofen, fentanyl, flavoxate, fluoxetine, fluphenazine, flurazepam, flurbiprofen, fluvoxamine, furosemide, glutethimide, glyburide, guaifenesin, haloperidol, homatropine, hydroalazine, hydrochlorothiazide, hydrocodone, hydromorphone, hydroxychloroquine, hydroxyzine, ibuprofen, imipramine, indomethacin, ketoconazole, ketoprofen, ketorolac, labetalol, levorphanol, lidocaine, loratadine, lorazepam, lovastatin, loxapine, mazindol, mefenamic acid, meperidine, mephenytoin, mepivacaine, mesoridazine, metaproterenol, methadone, methdilazine, methocarbamol, methotrexate, methotrimeprazine, methoxamine, methyl dopa, methylphenidate, metoclopramide, metolazone, metoprolol, metronidazole, midazolam, mocllobemide, morphine, nadolol, nalbuphine, naloxone, naphazoline, naproxen, nifedipine, nizatidine, norepinephrine, nortriptyline, oxazepam, oxycodone, oxymetazoline, paroxetine, pemoline, pentazocine, pentobarbital, pentoxifylline, perphenazine, pheniramine, phenobarbital, phenol, phenolphthalein, phentolamine, phenylbutazone, phenyltoloxamine, phenytoin, pimozone, pindolol, piroxicam, pramoxine, prazepam, prazosin, probenecid, procainamide, procaine, prochlorperazine, procyclidine, promazine, promethazine, propafenone, propantheline, propiomazine, propofol, propranolol, protriptyline, quazepam, quinidine, quinine, racemethorphan, ranitidine, remoxipride, risperidone, salicylic acid, scopolamine, secobarbital, sertraline, sotalol, spironolactone, sulfapyrazone, sulindac, temazepam, terbutaline, terfenadine, tetracaine, theophylline, thiethylperazine, thiopen-

tal, thioridazine, thiothixene, timolol, tocainide, tolbutamide, tolmetin, trazodone, triamterene, triazolam, trifluoperazine, triflupromazine, trimeprazine, trimethoprim, trimipramine, verapamil, warfarin, xylometazoline, yohimbine, zopiclone

KEY WORDS

also details of plasma extraction

REFERENCE

Koves,E.M. Use of high-performance liquid chromatography-diode array detection in forensic toxicology, *J.Chromatogr.A*, **1995**, 692, 103–119.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4.6 Sumchiral CSP 8 (Sumika Chemical Analysis Service)

Mobile phase: n-Hexane:1,2-dichloroethane:MeOH:trifluoroacetic acid 250:140:10:1

Flow rate: 1

Detector: UV 230-280

CHROMATOGRAM

Retention time: 33, 45 (enantiomers)

KEY WORDS

chiral

REFERENCE

Oi,N.; Kitahara,H.; Aoki,F. Direct enantiomer separations by high-performance liquid chromatography with chiral urea derivatives as stationary phases, *J.Chromatogr.A*, **1995**, 694, 129–134.

SAMPLE

Matrix: solutions

Sample preparation: Inject a 20 µL aliquot of a 100-500 µg/mL solution in mobile phase.

HPLC VARIABLES

Column: 100 × 4.6 5 µm Hypersil C8 MOS 100A coated with phosphatidylcholine (95% pure soybean lecithin, Epikuron, Lucas Meyer & Co.) (Coat column by recycling a 1 mM solution of phosphatidylcholine in MeOH:water 80:20 for 24 h.)

Mobile phase: MeCN:35 mM pH 7.4 sodium phosphate buffer 40:60

Flow rate: 0.5–2

Injection volume: 20

Detector: UV 254

CHROMATOGRAM

Retention time: k' 2.09

OTHER SUBSTANCES

Also analyzed: amoxicillin, antipyrine, carbamazepine, chlorpromazine, clonidine, codeine, desipramine, diphenhydramine, dipyridamole, ephedrine, flufenamic acid, haloperidol, hydroxyzine, imipramine, indomethacin, lidocaine, megestrol acetate, metoprolol, nabumetone, nadolol, phenobarbital, phenol, promazine, propranolol, pyrilamine, quinidine, ropinirole, testosterone, thioridazine, tolfenamic acid, verapamil

Noninterfering: acetaminophen, aspirin, azathioprine, caffeine, carprofen, chlorambucil, cimetidine, fenoterol, flurbiprofen, ibuprofen, ketoprofen, ranitidine, salicylic acid, sulfamethoxazole, theophylline, thioguanine, tiaprofenic acid, trimethoprim, valproic acid

KEY WORDScomparison with capillary electrophoresis

REFERENCE

Hanna,M.; de Biasi,V.; Bond,B.; Salter,C.; Hutt,A.J.; Camilleri,P. Estimation of the partitioning characteristics of drugs: A comparison of a large and diverse drug series utilizing chromatographic and electrophoretic methodology, *Anal.Chem.*, **1998**, 70, 2092–2099.

SAMPLE**Matrix:** urine

Sample preparation: 500 μ L Urine + N-ethylnordiazepam + 100 μ L buffer, centrifuge at 11000 g for 30 s, inject a 500 μ L aliquot onto column A with mobile phase A, after 0.6 min backflush column A with mobile phase A to waste for 1.6 min, elute column A with 250 μ L mobile phase B, with 200 μ L mobile phase C, and with 1.15 mL mobile phase D. Elute column A to waste until drugs start to emerge then elute onto column B. Elute column B to waste until drugs started to emerge, then elute onto column C. When all the drugs have emerged from column B remove it from the circuit, elute column C with mobile phase D, monitor the effluent from column C. Flush column A with 7 mL mobile phase E, with mobile phase D, and mobile phase A. Flush column B with 5 mL mobile phase E then with mobile phase D. (Buffer was 6 M ammonium acetate adjusted to pH 8.0 with 2 M KOH.)

HPLC VARIABLES

Column: A 10 \times 2.1 12-20 μ m PRP-1 spherical poly(styrene-divinylbenzene) (Hamilton); B 10 \times 3.2 11 μ m Aminex A-28 (Bio-Rad); C 25 \times 3.2 5 μ m C8 (Phenomenex) + 150 \times 4.6 5 μ m silica (Macherey-Nagel)

Mobile phase: A 0.1% pH 8.0 potassium borate buffer; B 6 mM KH_2PO_4 containing 5 mM tetramethylammonium hydroxide, and 2 mM dimethyloctylamine, pH adjusted to 6.50 with phosphoric acid; C MeCN:buffer 40:60 (Buffer was 6 mM KH_2PO_4 containing 5 mM tetramethylammonium hydroxide, and 2 mM dimethyloctylamine, pH adjusted to 6.50 with phosphoric acid.); D MeCN:buffer 33:67 (Buffer was 6 mM KH_2PO_4 containing 5 mM tetramethylammonium hydroxide, and 2 mM dimethyloctylamine, pH adjusted to 6.50 with phosphoric acid.); E MeCN:buffer 70:30 (Buffer was 6 mM KH_2PO_4 containing 5 mM tetramethylammonium hydroxide, and 2 mM dimethyloctylamine, pH adjusted to 6.50 with phosphoric acid.)

Column temperature: ambient (column A), 40 (columns B and C)

Flow rate: A 5; B-E 1

Injection volume: 500

Detector: UV 210, UV 235

CHROMATOGRAM

Retention time: k' 5.9

Internal standard: N-ethylnordiazepam (k' 2.1)

Limit of detection: 300 ng/mL

OTHER SUBSTANCES

Extracted: caffeine, cotinine, benzoylecgonine, secobarbital, oxazepam, phenobarbital, nordiazepam, diazepam, phenylpropanolamine, phentermine, amphetamine, phenmetrazine, lidocaine, ephedrine, pentazocine, methamphetamine, desipramine, nortriptyline, diphenhydramine, methadone, imipramine, flurazepam, amitriptyline, morphine, hydromorphone, hydrocodone

Interfering: codeine

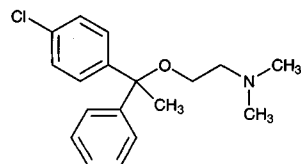
KEY WORDS

column-switching

REFERENCE

Binder,S.R.; Regalia,M.; Biaggi-McEachern,M.; Mazhar,M. Automated liquid chromatographic analysis of drugs in urine by on-line sample cleanup and isocratic multi-column separation, *J.Chromatogr.*, **1989**, 473, 325-341.

Chlorphenoxamine



Molecular formula: C₁₈H₂₂ClNO

Molecular weight: 303.83

CAS Registry No.: 77-38-3, 562-09-4 (HCl)

Merck Index: 2234

Lednicer No.: 1 44

SAMPLE

Matrix: solutions

Sample preparation: Prepare a 10 µg/mL solution in MeOH, inject a 20 µL aliquot.

HPLC VARIABLES

Column: 125 × 4.9 Spherisorb S5W silica

Mobile phase: MeOH containing 10 mM ammonium perchlorate and 1 mL/L 100 mM NaOH in MeOH, pH 6.7

Flow rate: 2

Injection volume: 20

Detector: E, LeCarbone, V25 glassy carbon electrode, + 1.2 V

CHROMATOGRAM

Retention time: 3.6

OTHER SUBSTANCES

Also analyzed: acebutolol, acepromazine, acetophenazine, N-acetylprocainamide, albuterol, alprenolol, amethocaine, amiodarone, amitriptyline, antazoline, atenolol, azacyclonal, bamethan, benactyzine, benperidol, benzethidine, benzocaine, benzoctamine, benzphetamine, benzquinamide, bromhexine, bromodiphenhydramine, bromperidol, brompheniramine, brompromazine, buclizine, bufotenine, bupivacaine, buprenorphine, butacaine, butethamate, chlorcyclizine, chlorpheniramine, chlorprenaline, chlorpromazine, chlorprothixene, cimetidine, cinchonidine, cinnarizine, clemastine, clomipramine, clonidine, cocaine, cyclazocine, cyclizine, cyclopentamine, cyproheptadine, deserpidine, desipramine, dextromoramide, dextropropoxyphene, dicyclomine, diethylcarbamazine, diethylpropion, diethylthiambutene, dihydroergotamine, dimethindene, dimethothiazine, diphenhydramine, diphenoxylate, dipipanone, diprenorphine, dipyrindamole, disopyramide, dothiepin, doxapram, doxepin, doxylamine, droperidol, ephedrine, ergocornine, ergocristine, ergocristinine, ergocryptine, ergometrine, ergosine, ergosinine, ergotamine, ethopropazine, etorphine, etoxeridine, fenethazine, fenfluramine, fenoterol, fentanyl, flavoxate, fluopromazine, flupenthixol, fluphenazine, flurazepam, haloperidol, hydroxyzine, hyoscine, ibogaine, imipramine, indapamine, iprindole, isothipendyl, isoxsuprine, ketanserine, laudanosine, lidocaine, lofepramine, loxapine, maprotiline, mecamlamine, meclophenoxate, meclozine, medazepam, mephentermine, mepivacaine, meptazinol, mepyramine, mesoridazine, metaraminol, methadone, methamphetamine, methapyrilene, methdilazene, methotrimeprazine, methoxamine, methoxyphenamine, methoxypromazine, methylephedrine, methylergonovine, methysergide, metoclopramide, metopimazine, metoprolol, mianserin, morazone, nadolol, nalorphine, naloxone, naphazoline, nicotine, nifedipine, nomifensine, nortriptyline, noscapine, orphenadrine, oxeladin, oxprenolol, oxymetazolin, papaverine, pargyline, pecazine, penbutolol, pentazocine, penthienate, pericyazine, perphenazine, phenadoxone, phenampromide, phenazocine, phenbutrazate, phendimetrazine, phenelzine, phenglutarimide, phenindamine, pheniramine, phenmetrazine, phenomorphan, phenoperidine, phenothiazine, phenoxybenzamine, phentolamine, phenylephrine, phenyltoloxamine, physostigmine, piminodine, pimozone, pindolol, pipamazine, pipazethate, piperacetazine, piperidolate, pipradol, pirenzepine, piritramide, pizotifen, practolol, pramoxine, prazosin, prenylamine, prilocaine, primaquine, proadifen, procainamide, procaine, prochlorperazine, procyclidine, proheptazine, prolintane, promazine, promethazine, pronethalol, properidine, propiomazine, propranolol, prothipendyl,

protriptyline, proxymetacaine, pseudoephedrine, pyrimethamine, quinidine, quinine, ranitidine, rescinnamine, sotalol, tacrine, terazosin, terbutaline, terfenadine, thenyldiamine, theophylline, thiethylperazine, thiopropazate, thioproperazine, thioridazine, thiothixene, thonzylamine, timolol, tocainide, tolpropamine, tolycaine, tranylcypromine, trazodone, tri-fluoperazine, trifluoperidol, trimeperidine, trimeprazine, trimethobenzamide, trimethoprim, trimipramine, tripeleppamine, triprolidine, tryptamine, verapamil, xylometazoline

REFERENCE

- Jane, I.; McKinnon, A.; Flanagan, R.J. High-performance liquid chromatographic analysis of basic drugs on silica columns using non-aqueous ionic eluents. II. Application of UV, fluorescence and electrochemical oxidation detection, *J.Chromatogr.*, **1985**, *323*, 191-225.

Chlorpromazine

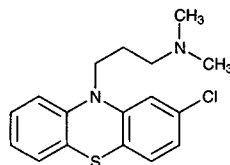
Molecular formula: C₁₇H₁₉ClN₂S

Molecular weight: 318.87

CAS Registry No.: 50-53-3, 69-09-0 (HCl)

Merck Index: 2238

Lednicer No.: 1 319



SAMPLE

Matrix: blood

Sample preparation: 2 mL Plasma + 1 mL 50 µg/mL mesoridazine in water + 100 µL 1 M HCl, vortex for 30 s, add 4 mL isopropanol, mix for 5 min, centrifuge at 5000 rpm at 0° for 20 min. Remove the supernatant and adjust the pH to 12.5 with 200 µL 5 M NaOH, mix for 10 s, add 4 mL n-heptane, mix for 10 min, centrifuge at 2500 rpm. Remove the organic layer and evaporate it to dryness under a stream of nitrogen, reconstitute the residue in 200 µL MeCN, mix for 2 min, inject a 75-100 µL aliquot.

HPLC VARIABLES

Column: 250 × 3.2 5 µm Spherisorb CN

Mobile phase: MeCN:15 mM pH 6.5 acetate buffer 90:10

Flow rate: 1.6

Injection volume: 75-100

Detector: UV 254

CHROMATOGRAM

Retention time: 1.9

Internal standard: mesoridazine (7)

Limit of quantitation: 1 ng/mL

OTHER SUBSTANCES

Extracted: metabolites

KEY WORDS

plasma; pharmacokinetics

REFERENCE

Midha,K.K.; Cooper,J.K.; McGilveray,I.J.; Butterfield,A.G.; Hubbard,J.W. High-performance liquid chromatographic assay for nanogram determination of chlorpromazine and its comparison with a radioimmunoassay, *J.Pharm.Sci.*, **1981**, *70*, 1043-1046.

SAMPLE

Matrix: blood

Sample preparation: 1-5 mL Plasma + 1 mL 1 M NaOH + hexanes, extract for 30 min, centrifuge. Remove a 9 mL aliquot of the organic phase and evaporate it to dryness at 30° under a stream of nitrogen. Dissolve the residue in 100 µL mobile phase, inject a 50 µL aliquot.

HPLC VARIABLES

Column: 10 µm Micropak CN (Varian)

Mobile phase: MeCN:5 mM ammonium acetate 90:10

Flow rate: 2.5

Injection volume: 50

Detector: UV 254

CHROMATOGRAM

Retention time: 21.7

Limit of detection: 10 ng/mL

OTHER SUBSTANCES

Simultaneous: acetophenazine, amitriptyline, benztropine, butaperazine, carphenazine, fluphenazine, promethazine, haloperidol, imipramine, mesoridazine, nortriptyline, orphenadrine, piperacetazine, promazine, thioridazine, thiothixene, trifluoperazine, trifluorpromazine, trihexyphenidyl, trimeprazine, metabolites

KEY WORDS

plasma

REFERENCE

Curry, S.H.; Brown, E.A.; Hu, O.Y.-P.; Perrin, J.H. Liquid chromatographic assay of phenothiazine, thioxanthene and butyrophenone neuroleptics and antihistamines in blood and plasma with conventional and radial compression columns and UV and electrochemical detection, *J.Chromatogr.*, **1982**, 231, 361–376.

SAMPLE

Matrix: blood

Sample preparation: 2 mL Plasma + 1 mL 100 ng/mL prochlorperazine in water, vortex for 10 s, add 500 μ L saturated sodium carbonate, vortex, add 5 mL pentane:isopropanol 97:3, mix for 20 min, centrifuge at 1725 g for 5 min, remove the organic layer and repeat the extraction. Combine the organic layers and evaporate them to dryness at 65° after adding a few anti-bumping granules. Cool, add 200 μ L MeCN, mix for 20 s, inject a 100 μ L aliquot.

HPLC VARIABLES

Column: 250 \times 4.6 10 μ m Spherisorb CN

Mobile phase: MeCN:100 mM ammonium acetate 90:10

Flow rate: 4

Injection volume: 100

Detector: E, Bioanalytical Systems Model LC4A, glassy carbon electrode +0.9 V, fixed 10 nA feed

CHROMATOGRAM

Retention time: 2.4

Internal standard: prochlorperazine (4.4)

Limit of detection: 0.1 ng/mL

Limit of quantitation: 0.25 ng/mL

KEY WORDS

plasma

REFERENCE

Cooper, J.K.; McKay, G.; Midha, K.K. Subnanogram quantitation of chlorpromazine in plasma by high-performance liquid chromatography with electrochemical detection, *J.Pharm.Sci.*, **1983**, 72, 1259–1262.

SAMPLE

Matrix: blood

Sample preparation: 2 mL Plasma + 100 μ L 1 μ g/mL loxapine in isopropanol:diethylamine 99.9:0.1 + 250 μ L 25% potassium carbonate containing 0.1% diethylamine + 5 mL hexane:isoamyl alcohol 97:3, vortex for 30 s, centrifuge at 500 g for 3 min. Remove the organic layer and add it to 100 μ L 250 mM HCl, vortex for 30 s, inject a 50 μ L aliquot of the aqueous phase.

HPLC VARIABLES

Guard column: 50 \times 4.6 40 μ m C8 (Supelco)

Column: 250 × 4.6 5 μm Supelcosil C8

Mobile phase: MeCN:water:diethylamine:85% phosphoric acid 53.3:45.1:1:0.4, pH adjusted to 7.2 with NaOH or phosphoric acid

Flow rate: 2

Injection volume: 50

Detector: UV 254

CHROMATOGRAM

Retention time: k' 8.23

Internal standard: loxapine (k' 7.18)

OTHER SUBSTANCES

Extracted: amitriptyline, chlordiazepoxide, desipramine, desmethldiazepam, desmethyl-chlordiazepoxide, desmethyldoxepin, diazepam, doxepin, fluphenazine, haloperidol, imipramine, nortriptyline, oxazepam, thiothixene

Noninterfering: molindone, perphenazine, trifluoperazine

KEY WORDS

plasma

REFERENCE

Kiel, J.S.; Abramson, R.K.; Morgan, S.L.; Voris, J.C. A rapid high performance liquid chromatographic method for the simultaneous measurement of six tricyclic antidepressants, *J. Liq. Chromatogr.*, **1983**, 6, 2761–2773.

SAMPLE

Matrix: blood

Sample preparation: 2 mL Plasma + 200 μL 5 M NaOH + 10 mL chloroform, shake for 10 min, stand in an ice bath for at least 30 min, centrifuge at 4° at 2800 rpm (RCF = 1578) for 10 min. Remove the organic layer and evaporate it under nitrogen at 40°. Dissolve the residue in 200 μL mobile phase, inject.

HPLC VARIABLES

Column: 250 × 4.6 5 μm Spherisorb nitrile

Mobile phase: MeCN:100 mM (NH₄)H₂PO₄ + 50 mg/L EDTA adjusted to pH 6.5 with ammonia 60:40

Flow rate: 2

Injection volume: 200

Detector: E, Bioanalytical Systems LC-4B, glassy carbon electrode 0.85 V

CHROMATOGRAM

Retention time: 4

Internal standard: chlorpromazine

OTHER SUBSTANCES

Simultaneous: prochlorperazine

KEY WORDS

plasma; chlorpromazine is IS

REFERENCE

Fowler, A.; Taylor, W.; Bateman, D.N. Plasma prochlorperazine assay by high-performance liquid chromatography-electrochemistry, *J. Chromatogr.*, **1986**, 380, 202–205.

SAMPLE

Matrix: blood

Sample preparation: 1 mL Plasma + 1 mL water, vortex for a few s, add 500 μ L 650 mM sodium carbonate, vortex for a few s, add 7 mL pentane:ethyl acetate 75:25, mix for 15 min, let stand for 5 min. Remove the upper organic layer and evaporate it to dryness under a stream of nitrogen at 65°, reconstitute the residue in 40 μ L MeCN, mix for a few s, inject a 30 μ L aliquot.

HPLC VARIABLES

Column: 150 \times 4.6 Spherisorb cyano

Mobile phase: MeCN:MeOH:100 mM pH 7 ammonium acetate 90:5:5

Flow rate: 1.5

Injection volume: 30

Detector: E, ESA 5100A, Model 5020 guard cell +1.00 V, model 5011 analytical cell, cell 1 +0.50 V, cell 2 +0.75 V

CHROMATOGRAM

Retention time: 10.87

Internal standard: chlorpromazine

OTHER SUBSTANCES

Extracted: fluphenazine

KEY WORDS

plasma; chlorpromazine is IS

REFERENCE

Cooper, J.K.; Hawes, E.M.; Hubbard, J.W.; McKay, G.; Midha, K.K. An ultrasensitive method for the measurement of fluphenazine in plasma by high-performance liquid chromatography with coulometric detection, *Ther. Drug Monit.*, **1989**, *11*, 354–360.

SAMPLE

Matrix: blood

Sample preparation: 1 mL Serum + 1 mL 650 mM sodium carbonate, vortex, add 7 mL pentane:ethyl acetate 50:50, shake vigorously for 15 min, centrifuge at 1110 g for 10 min. Remove the organic layer and evaporate it to dryness at 65° under nitrogen. Reconstitute the residue in 300 μ L MeCN:MeOH:isopropanol:water: 1 M ammonium acetate pH 5.0 83:5:5:6.65:0.35, sonicate for 5 min, vortex for 30 s, inject a 100 μ L aliquot.

HPLC VARIABLES

Column: 150 \times 4.6 5 μ m Burdick & Jackson CN

Mobile phase: MeCN:MeOH:isopropanol:water: 1 M ammonium acetate pH 7.2 83:5:5:6.65:0.35

Flow rate: 1.5

Injection volume: 100

Detector: E, ESA Model 5100A Coulochem detector, Model 5011 analytical cell, detector 1 +0.50 V, detector 2 +0.70 V

CHROMATOGRAM

Retention time: 10.2

Internal standard: chlorpromazine

OTHER SUBSTANCES

Simultaneous: promethazine

KEY WORDS

serum; chlorpromazine is IS

REFERENCE

Fox,A.R.; McLoughlin,D.A. Rapid, sensitive high-performance liquid chromatographic method for the quantification of promethazine in human serum with electrochemical detection, *J.Chromatogr.*, **1993**, *631*, 255-259.

SAMPLE

Matrix: blood

Sample preparation: 1 mL Plasma + 100 μ L 200 ng/mL IS in MeOH + 1 mL 50 mM pH 10 borate buffer, vortex briefly, add to an Extrelut 3 SPE cartridge, let stand for 5 min, elute with 15 mL hexane:dichloromethane 50:50. Add the eluate to 3 mL 50 mM sulfuric acid, mix for 10 min, centrifuge at 3000 g for 10 min. Remove the aqueous layer and add it to 6 mL hexane:dichloromethane 50:50, wash for 5 min, centrifuge. Make the aqueous layer basic with 150 μ L 28% ammonia, extract twice with 3 mL hexane:dichloromethane 50:50. Combine the organic layers and evaporate them to dryness under a stream of nitrogen at 60°, reconstitute the residue in 100 μ L mobile phase, inject a 20 μ L aliquot.

HPLC VARIABLES

Guard column: 30 \times 4.6 5 μ m Spherisorb cyano

Column: 250 \times 4.6 5 μ m Ultrasphere cyano

Mobile phase: MeCN:buffer 60:40 (Buffer was 50 mM KH_2PO_4 adjusted to pH 6.5 with 28% ammonia.)

Flow rate: 1

Injection volume: 20

Detector: E, 5100 A Coulochem, 5020 guard cell 1.00 V, 5011 analytical cell, detector 1 0.55 V, detector 2 0.80 V, output of detector 2 is monitored

CHROMATOGRAM

Retention time: 26.4

Internal standard: methylrisperidone (R68808) (14.3)

OTHER SUBSTANCES

Extracted: clomipramine, cyamemazine, desipramine, droperidol, flunitrazepam, haloperidol, imipramine, pipamperone, risperidone, trihexyphenidyl

Noninterfering: alprazolam, bromazepam, carbamazepine, chlorazepate, diazepam, diphenylhydantoin, estazolam, ethylbenzatropine, oxazepam, phenobarbital, triazolam, valproic acid

KEY WORDS

plasma; SPE

REFERENCE

Le Moing,J.P.; Edouard,S.; Levron,J.C. Determination of risperidone and 9-hydroxyrisperidone in human plasma by high-performance liquid chromatography with electrochemical detection, *J.Chromatogr.*, **1993**, *614*, 333-339.

SAMPLE

Matrix: blood

Sample preparation: Automated SPE by ASPEC system. Condition a C18 Clean-Up SPE cartridge (CEC 18111, Worldwide Monitoring) with 2 mL MeOH then 2 mL water. 1 mL Plasma + 1 mL 400 ng/mL protriptyline in water, vortex, add to column, wash with 3 mL water, wash with 3 mL 750 mL/L methanol. Elute with three aliquots of 300 μ L 0.1 M ammonium acetate in MeOH. Add 0.5 mL 0.5 M NaOH and 4 mL 50 mL/L isopropanol in heptane to eluate, mix thoroughly. Allow 5 min for phase separation. Remove upper heptane phase and add it to 300 μ L 0.1 M phosphoric acid (pH 2.5), mix, separate, inject a 100 μ L aliquot of the aqueous phase.

HPLC VARIABLES

Guard column: LC-8-DB (Supelco)

Column: 150 × 4.6 LC-8-DB (Supelco)

Mobile phase: MeCN:buffer 35:65 (Buffer was 10 mL/L triethylamine in water adjusted to pH 5.5 with glacial acetic acid.)

Flow rate: 2

Injection volume: 100

Detector: UV 228

CHROMATOGRAM

Retention time: 7.0

Internal standard: protriptyline (4)

OTHER SUBSTANCES

Extracted: acetazolamide, amitriptyline, chlordiazepoxide, chlorimipramine, desipramine, dextromethorphan, diazepam, diphenhydramine, doxepin, encainide, fentanyl, flecainide, fluoxetine, flurazepam, haloperidol, hydroxyethylflurazepam, ibuprofen, imipramine, lidocaine, maprotiline, methadone, methaqualone, mexiletine, midazolam, nordoxepin, nordiazepam, norfluoxetine, nortriptyline, norverapamil, pentazocine, promazine, propafenone, propoxyphene, propranolol, protriptyline, quinidine, temazepam, trazodone, trimipramine, verapamil

Noninterfering: acetaminophen, acetylmorphine, amiodarone, amobarbital, amphetamine, bendroflumethiazide, benzocaine, benzoylecgonine, benzthiazide, butalbital, carbamazepine, chlorothiazide, clonazepam, cocaine, codeine, cotinine, cyclosporine, cyclothiazide, desalkylflurazepam, diamorphine, dicumerol, ephedrine, ethacrynic acid, ethanol, ethchlorvynol, ethosuximide, furosemide, glutethimide, hydrochlorothiazide, hydrocodone, hydroflumethiazide, hydromorphone, lorazepam, mephentermine, meprobamate, methamphetamine, metharbital, methoxsalen, methoxyphenteramine, methsuximide, methylcyclothiazide, metoprolol, MHPG, monoacetylmorphine, morphine, normethsuximide, oxazepam, oxycodone, oxymorphone, pentobarbital, phenacyclidine, phenteramine, phenylephrine, phenytoin, polythiazide, primidone, prochlorperazine, salicylic acid, sulfanilamide, THC-COOH, theophylline, thiazolam, thiopental, thioridazine, tocinide, trichloromethiazide, trifluoperazine, valproic acid, warfarin

Interfering: norchlorimipramine

KEY WORDS

plasma; SPE

REFERENCE

Nichols, J.H.; Charlson, J.R.; Lawson, G.M. Automated HPLC assay of fluoxetine and norfluoxetine in serum, *Clin. Chem.*, **1994**, *40*, 1312–1316.

SAMPLE

Matrix: blood

Sample preparation: 2 mL Whole blood or plasma + 2 mL buffer + 5 mL chloroform: isopropanol:n-heptane 60:14:26, shake gently horizontally for 10 min, centrifuge at 2800 g for 10 min. Remove the lower organic layer and evaporate it to dryness under vacuum at 45°, reconstitute the residue in 100 µL mobile phase, centrifuge at 2800 g for 5 min, inject a 50 µL aliquot of the supernatant. (Buffer was saturated ammonium chloride solution 25% diluted with water, adjusted to pH 9.5 with 25% ammonia solution.)

HPLC VARIABLES

Column: 300 × 3.9 4 µm NovaPack C18

Mobile phase: MeOH:THF:buffer 65:5:30 (Buffer was 0.68 g/L (10 mM (sic)) KH₂PO₄ adjusted to pH 2.6 with concentrated orthophosphoric acid.) (At the end of each session wash the column with water for 1 h and MeOH for 1 h, re-equilibrate for 30 min.)

Column temperature: 30

Flow rate: 0.8

Injection volume: 50**Detector:** UV 256**CHROMATOGRAM****Retention time:** 11.50**Limit of detection:** <120 ng/mL**KEY WORDS**

whole blood; plasma; interferences may occur—compounds(all of which are extracted) elute in this order tenoxicam; iproniazid; methocarbamol; methotrexate; caffeine; nialamide; colchicine; cytarabine; benzoylecgonine; acetaminophen; diazoxide; dacarbazine; sulfinpyrazole; flumazenil; sulpride; morphine; atenolol; toloxatone; terbutaline; albuterol; phenobarbital; ranitidine; tiapride; phenol; chlormezanone; aspirin; metformin; ritodrine; codeine; sultopride; amisulpride; naltrexone; lisinopril; benzocaine; nizatidine; nalorphine; mephnesin; naloxone; sotalol; carteolol; procainamide; carbamazepine; bromazepam; nalbuphine; nadolol; procarbazine; dihydralazine; omeprazole; strychnine; acebutolol; glutethimide; chlorpropamide; glipizide; triazolam; prazosin; flunitrazepam; clonazepam; metoclopramide; melphalan; estazolam; tolbutamide; ephedrine; clonidine; pindolol; clobazam; minoxidil; disopyramide; nitrazepam; dextromethorphan; tofisopam; zopiclone; debrisoquine; sulindac; alprazolam; cycloguanil; lorazepam; methaqualone; ketamine; piroxicam; metoprolol; nifedipine; quinine; mephentermine; prilocaine; pentazocine; oxazepam; tiaprofenic acid; quinidine; celiprolol; ajmaline; yohimbine; lidocaine; secobarbital; viloxazine; mepivacaine; meperidine; doxylamine; labetalol; temazepam; amodiaquine; benperidol; droperidol; hydroxychloroquine; zolpidem; ketoprofen; alminoprofen; cicletanine; moclobemide; chloroquine; cocaine; timolol; nomifensine; ticlopidine; acenocumarol; videsine; mexiletine; dipyridamole; trazodone; pipamperone; pyrimethamine; benazepril; vincristine; metapramine; chlordiazepoxide; oxprenolol; warfarin; clorazepate; flecainide; phenacyclidine; thiopental; fenfluramine; metipranolol; triprolidine; naproxen; buprenorphine; verapamil; buspirone; tianeptine; midazolam; bupivacaine; carbinoxamine; loperazolam; cetirizine; chlorpheniramine; moperone; cibenzoline; medifoxamine; astemizole; vinblastine; nicardipine; bisoprolol; diltiazem; glibornuride; reserpine; aconitine; nitrendipine; diazepam; mianserin; ramipril; haloperidol; tetracaine; alprenolol; aceprometazine; glibenclamide; chlorophenacinone; doxepin; nimodipine; diphenhydramine; cyclizine; histapyrrodine; phenylbutazone; demexiptiline; clozapine; proguanil; trifluoperidol; medazepam; cyamemazine; bumadizone; suriclone; propranolol; acepromazine; dothiepin; dextromoramide; fenoprofen; dextropropoxyphene; loxapine; betaxolol; propafenone; promethazine; thioproperazine; methadone; amoxapine; quinupramine; opipramol; cyproheptadine; brompheniramine; mefenidramine; protriptyline; flurbiprofen; tetrazepam; zorubicin; prazepam; alimemazine; loperamide; imipramine; desipramine; levomepromazine; hydroxyzine; niflumic acid; penbutolol; fluvoxamine; pimozone; daunorubicin; indomethacin; maprotiline; tropatenine; etodolac; fluoxetine; amitriptyline; nortriptyline; tiocloamarol; diclofenac; mefloquine; trimipramine; chlorambucil; lidoflazine; ibuprofen; floctafenine; alpidem; loratadine; chlorpromazine; clomipramine; carpipramine; thioridazine; fentiazac; clemastine; mefenamic acid; fluphenazine; prochlorperazine; penfluridol; bepridil; terfenadine; trifluoperazine

REFERENCE

Tracqui,A.; Kintz,P.; Mangin,P. Systematic toxicological analysis using HPLC/DAD, *J.Forensic Sci.*, **1995**, *40*, 254–262.

SAMPLE

Matrix: blood, gastric contents, tissue, urine

Sample preparation: 1 mL Blood, urine, or gastric contents or 1 g tissue homogenate + 500 μ L buffer + 8 mL n-hexane:ethyl acetate 70:30, mix on a rotary mixer for 10 min, centrifuge at 3000 g for 8 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen, reconstitute the residue in 100 μ L 12.5 mM NaOH in MeOH: water 50:50, inject a 50 μ L aliquot. (Buffer was 13.8 g potassium carbonate in 100 mL water, pH adjusted to 9.5 with concentrated HCl.)

HPLC VARIABLES

Guard column: 4 × 4 30 µm LiChrocart Aluspher RP-select B (Merck)

Column: 125 × 4 5 µm Aluspher RP-select B (Merck)

Mobile phase: Gradient. A was 12.5 mM NaOH in MeOH. B was 12.5 mM NaOH in water. A:B 10:90 for 5 min, to 90:10 over 15 min, maintain at 90:10 for 5 min, return to initial conditions over 1 min, re-equilibrate for 5 min.

Flow rate: 1

Injection volume: 50

Detector: UV 230, 254

CHROMATOGRAM

Retention time: 21

OTHER SUBSTANCES

Extracted: alprenolol, amitriptyline, bromazepam, carbamazepine, chlordiazepoxide, clonazepam, desipramine, diazepam, flunitrazepam, haloperidol, nitrendipine, nordiazepam, nortriptyline, pindolol, zolpidem

Also analyzed: acebutolol, acetaminophen, alprazolam, amphetamine, atenolol, betaxolol, brotizolam, caffeine, camazepam, captopril, chloroquine, clobazam, clomipramine, clothiapine, clotiazepam, cloxazolam, cocaine, codeine, diclofenac, dihydralazine, dihydrocodeine, dihydroergotamine, diphenhydramine, domperidone, doxepin, droperidol, ergotamine, ethyl loflazepate, fenethylline, fluoxetine, flupentixol, flurazepam, furosemide, glidazide, hydrochlorothiazide, hydroxyzine, ibuprofen, imipramine, ketazolam, loprazolam, lorazepam, lormetazepam, maprotiline, medazepam, mepyramine, methadone, methaqualone, methyl dopa, methylphenidate, metoclopramide, metoprolol, mexiletine, mianserin, midazolam, minoxidil, morphine, nadolol, nitrazepam, oxprenolol, papaverine, pentazocine, phenprocoumon, phenylbutazone, pipamperone, piritramide, practolol, prazepam, prazosin, promazine, promethazine, propoxyphene, propranolol, prothipendyl, quinine, sotalol, sulpride, thioridazine, trazodone, triazolam, trimipramine, tripeleminamine, tyramine, verapamil, yohimbine

REFERENCE

Lambert, W.E.; Meyer, E.; De Leenheer, A.P. Systematic toxicological analysis of basic drugs by gradient elution of an alumina-based HPLC packing material under alkaline conditions, *J. Anal. Toxicol.*, **1995**, *19*, 73–78.

SAMPLE

Matrix: blood, milk

Sample preparation: Condition a Sep-Pak C18 SPE cartridge with 5 mL MeOH and 5 mL water. 1 mL Serum or milk + 5 µL 100 µg/mL methotrimeprazine in MeOH + 5 mL 0.5 (serum) or 1 (milk) M HCl, mix, add to the SPE cartridge, wash with 5 mL water, wash with 5 mL MeOH:water 20:80, elute with 5 mL MeOH:water 60:40, evaporate eluate to dryness under vacuum at 60°, dissolve residue in 100 µL mobile phase, inject whole amount.

HPLC VARIABLES

Column: 150 × 4.6 5 µm Develosil C8-5 (Nomura)

Mobile phase: MeCN:0.5% KH₂PO₄ adjusted to pH 4.5 with 50% phosphoric acid 35:65

Flow rate: 1

Injection volume: 100

Detector: UV 254

CHROMATOGRAM

Retention time: 13

Internal standard: methotrimeprazine (levomepromazine) (10)

Limit of detection: 5 ng/mL

Limit of quantitation: 10 ng/mL

KEY WORDS

serum; SPE

REFERENCE

Ohkubo,T.; Shimoyama,R.; Sugawara,K. Determination of chlorpromazine in human breast milk and serum by high-performance liquid chromatography, *J.Chromatogr.*, **1993**, 614, 328–332.

SAMPLE**Matrix:** blood, tissue

Sample preparation: Blood or serum. 1 mL Blood or serum + 1 µg cianopramine + 1 mL water, vortex, add 1 mL 200 mM sodium carbonate, vortex, add 6 mL hexane:1-butanol 95:5, gently agitate for 30 min, centrifuge at 2500 g for 5 min. Remove the organic layer and add it to 100 µL 0.2% phosphoric acid, agitate gently for 30 min, centrifuge for 5 min. Remove the organic layer and inject a 30 µL aliquot of the aqueous layer. Liver homogenate. 0.5 mL Liver homogenate + 10 µg cianopramine + 500 µL 2% sodium tetraborate + 8 mL hexane:1-butanol 95:5, gently agitate for 30 min, centrifuge at 2500 g for 5 min. Remove the organic layer and add it to 400 µL 0.2% phosphoric acid, agitate gently for 30 min, centrifuge for 5 min. Remove the organic layer and inject a 30 µL aliquot of the aqueous layer.

HPLC VARIABLES**Guard column:** 15 × 3.2 7 µm RP-18 Newguard (Applied Biosystems)**Column:** 100 × 4.6 5 µm Brownlee Spheri-5 RP-18**Mobile phase:** MeCN:100 mM NaH₂PO₄:diethylamine 40:57.5:2.5**Flow rate:** 2**Injection volume:** 30**Detector:** UV 220

CHROMATOGRAM**Retention time:** 39.19**Internal standard:** cianopramine (8.93)

OTHER SUBSTANCES

Simultaneous: amitriptyline, amoxapine, benztropine, brompheniramine, chlorpheniramine, clomipramine, cyproheptadine, desipramine, diphenhydramine, dothiepin, doxepin, fluoxetine, haloperidol, imipramine, loxapine, maprotiline, meperidine, mesoridazine, methadone, metoclopramide, mianserin, moclobemide, nomifensine, nordoxepin, norfluoxetine, norpropoxyphene, northiaden, nortriptyline, pentobarbital, pheniramine, promethazine, propoxyphene, propranolol, protriptyline, quinidine, quinine, sulforidazine, thioridazine, thiothixene, tranilcypromine, trazodone, trihexiphenidyl, trimipramine, triprolidine

Noninterfering: dextromethorphan, norphethidine, phenoxybenzamine, prochlorperazine, trifluoperazine

KEY WORDS

serum; whole blood; liver

REFERENCE

McIntyre,I.M.; King,C.V.; Skafidis,S.; Drummer,O.H. Dual ultraviolet wavelength high-performance liquid chromatographic method for the forensic or clinical analysis of seventeen antidepressants and some selected metabolites, *J.Chromatogr.*, **1993**, 621, 215–223.

SAMPLE**Matrix:** blood, urine

Sample preparation: Plasma. 1 mL Plasma + 4 mL water + 1 mL 160 ng/mL thioridazine + 0.8 mL 1 M NaOH + 15 mL n-heptane:isoamyl alcohol 98.5:1.5, shake for 10 min, centrifuge at 700 g, remove the organic layer, repeat the extraction twice more. Combine

the organic layers and evaporate them to dryness, reconstitute the residue in 10 mL 50 mM HCl, add 20 mL diethyl ether, shake for 3 min. Remove the aqueous layer and make it alkaline with 1 mL 5 M NaOH, add 10 mL n-heptane:isoamyl alcohol 98.5:1.5, shake for 10 min, centrifuge at 700 g. Remove the organic layer and evaporate it to dryness, dissolve the residue in 1 mL MeCN, inject a 50 μ L aliquot. Urine. 20 mL Urine + 3 mL 1 M HCl + 1 mL 1 μ g/mL thioridazine, wash with diethyl ether, make the aqueous layer alkaline with 5 M NaOH, add n-heptane:isoamyl alcohol 98.5:1.5, shake for 10 min, centrifuge at 700 g. Remove the organic layer and evaporate it to dryness, dissolve the residue in 1 mL MeCN, inject a 10 μ L aliquot.

HPLC VARIABLES

Column: 150 \times 4.5 μ m Nucleosil C18

Mobile phase: MeCN:pyridine:THF:100 mM pH 3.5 acetate buffer 68.9:0.1:1:30 containing 20 mM sodium perchlorate

Flow rate: 0.7

Injection volume: 10-50

Detector: E, Yanaco Model VMD-101, glassy carbon working electrode 0.95 V, Ag/AgCl reference electrode

CHROMATOGRAM

Retention time: 8.0

Internal standard: thioridazine (9.5)

Limit of detection: 0.5 ng/mL (urine), 2 ng/mL (plasma)

OTHER SUBSTANCES

Extracted: methotrimeprazine (levomepromazine)

KEY WORDS

plasma

REFERENCE

Murakami, K.; Ueno, T.; Hijikata, J.; Shirasawa, K.; Muto, T. Simultaneous determination of chlorpromazine and levomepromazine in human plasma and urine by high-performance liquid chromatography using electrochemical detection, *J. Chromatogr.*, **1982**, 227, 103-112.

SAMPLE

Matrix: blood, urine

Sample preparation: Add 1 mL whole blood or urine to Toxi-Tube A (Toxi-Lab, Irvine CA), add 3 mL water, mix by gentle inversion for 5 min, centrifuge at 1500 g for 5 min. Remove the organic layer and evaporate it to dryness under a stream of nitrogen at 40°, reconstitute the residue with 50 μ L MeCN:water 50:50, vortex for 10 s, centrifuge at 7500 g for 2 min, inject a 10 (urine) or 30 (blood) μ L aliquot. (The detector wavelength shown is the wavelength of maximum absorbance. This will not necessarily be the optimal wavelength for the separation. Multiple wavelengths from 200-350 nm can be scanned using a diode-array detector. Otherwise, 220 nm may be a reasonable choice for initial work. Matrix may interfere.)

HPLC VARIABLES

Guard column: 20 mm long Symmetry C18

Column: 250 \times 4.6 μ m Symmetry C8 (Waters)

Mobile phase: Gradient. A was 50 mM pH 3.8 sodium phosphate buffer. B was MeCN. A: B 85:15 for 6.5 min, 65:35 for 18.5 min, 20:80 for 3 min (step gradient), re-equilibrate at initial conditions for 7 min.

Column temperature: 30

Flow rate: 1 for 6.5 min, to 1.5 over 18.5 min, maintain at 1.5 for 3 min (re-equilibrate at 1.5 mL/min)

Injection volume: 10-30

Detector: UV 254.7

CHROMATOGRAM

Retention time: 16.035

KEY WORDS

whole blood

REFERENCE

Gaillard,Y.; Pépin,G. Use of high-performance liquid chromatography with photodiode-array UV detection for the creation of a 600-compound library. Application to forensic toxicology, *J.Chromatogr.A*, **1997**, 763, 149–163.

SAMPLE

Matrix: formulations

Sample preparation: Crush tablet or capsule, to 2 mg amitriptyline add 20 mL MeOH, shake 30 min, centrifuge at 2000 rpm for 5 min, to 5 mL supernatant add 4 mL 1.25 mg/mL norephedrine.HCl in MeOH, dilute to 10 mL with MeOH.

HPLC VARIABLES

Column: 150 × 4.6 5 µm Zorbax CN

Mobile phase: MeCN:MeOH:25 mM pH 4.8 sodium acetate-acetic acid buffer 35:45:20

Flow rate: 2.5

Injection volume: 10

Detector: UV 254

CHROMATOGRAM

Retention time: 5.1

Internal standard: Norephedrine (2.7)

OTHER SUBSTANCES

Also analyzed: amitriptyline, imipramine, thioridazine, trifluoperazine

KEY WORDS

tablets; capsules

REFERENCE

Lovering,E.G.; Beaulieu,N.; Lawrence,R.C.; Sears,R.W. Liquid chromatographic method for identity, assay, and content uniformity of five tricyclic drugs, *J.Assoc.Off.Anal.Chem.*, **1985**, 68, 168–171.

SAMPLE

Matrix: formulations

Sample preparation: Inject a 20 µL aliquot.

HPLC VARIABLES

Column: 250 × 4 Zorbax ODS

Mobile phase: MeOH containing 0.5 g/L sodium acetate

Column temperature: 35

Flow rate: 1.5

Injection volume: 20

Detector: UV 228

CHROMATOGRAM

Retention time: 5.0

OTHER SUBSTANCES

Simultaneous: trifluoperazine, trihexyphenidyl

REFERENCE

Pradas,T.N.V.; Sivakumar,M. HPLC quantification of a tricomponent psychiatric formulation containing chlorpromazine, trifluoperazine and trihexyphenidyl, *Pharmazie*, **1992**, 47, 231-231.

SAMPLE

Matrix: hair

Sample preparation: Wash hair in water, rinse 3 times with MeOH, dry, weigh. 5-25 mg Washed hair + 1 mL 1 M NaOH, heat at 70° for 30 min, adjust pH to 9.5-10. 1 mL Extract + 1 µg protriptyline + 1 mL water + 1 mL 200 mM sodium carbonate buffer, mix, extract with hexane:butanol 95:5 for 20 min. Remove the organic layer and add it to 100 µL 0.2% orthophosphoric acid, mix for 20 min, inject a 30 µL aliquot of the aqueous layer.

HPLC VARIABLES

Column: 150 × 3.9 5 µm Nova-Pak phenyl

Mobile phase: MeCN:buffer 55:45 (Buffer was 10 mM pH 3.0 KH₂PO₄.)

Flow rate: 1.5

Injection volume: 30

Detector: UV 255

CHROMATOGRAM

Internal standard: protriptyline (UV 214) (4)

OTHER SUBSTANCES

Extracted: thioridazine (UV 265)

REFERENCE

Couper,F.J.; McIntyre,I.M.; Drummer,O.H. Extraction of psychotropic drugs from human scalp hair, *J.Forensic Sci.*, **1995**, 40, 83-86.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 150 × 4.6 5 µm LiChrosphere 100RP-18

Mobile phase: MeOH:25% (w/w) ammonia 99.2:0.8

Flow rate: 1.2

Injection volume: 20

Detector: UV 258

CHROMATOGRAM

Retention time: k' 2.78

OTHER SUBSTANCES

Simultaneous: carbetapentane

REFERENCE

Gad-Kariem,E.A.; Abounassif,M.A. Determination of pentoxyverine in cough preparations by high performance liquid chromatography, *J.Liq.Chromatogr.Rel.Technol.*, **1997**, 20, 3049-3059.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4 ODS (Hitachi)

Mobile phase: MeCN:50 mM phosphoric acid 50:50 containing 300 mM KCl

Column temperature: 55

Flow rate: 0.6**Injection volume:** 20**Detector:** UV 255

OTHER SUBSTANCES**Also analyzed:** amitriptyline, clomipramine, promazine, promethazine, thymol

REFERENCE

Sugawara, M.; Takekuma, Y.; Yamada, H.; Kobayashi, M.; Iseki, K.; Miyazaki, K. A general approach for the prediction of the intestinal absorption of drugs: regression analysis using the physicochemical properties and drug-membrane electrostatic interactions, *J. Pharm. Sci.*, **1998**, *87*, 960–966.

SAMPLE**Matrix:** solutions**Sample preparation:** Prepare a 10 µg/mL solution in MeOH, inject a 20 µL aliquot.

HPLC VARIABLES**Column:** 125 × 4.9 Spherisorb S5W silica**Mobile phase:** MeOH containing 10 mM ammonium perchlorate and 1 mL/L 100 mM NaOH in MeOH, pH 6.7**Flow rate:** 2**Injection volume:** 20**Detector:** E, LeCarbone, V25 glassy carbon electrode, + 1.2 V

CHROMATOGRAM**Retention time:** 4.4

OTHER SUBSTANCES

Also analyzed: acebutolol, acepromazine, acetophenazine, N-acetylprocainamide, albuterol, alprenolol, amethocaine, amiodarone, amitriptyline, antazoline, atenolol, azacyclonal, bamethan, benactyzine, benperidol, benzethidine, benzocaine, benzocetamine, benzphetamine, benzquinamide, bromhexine, bromodiphenhydramine, bromperidol, brompheniramine, brompromazine, buclizine, bufotenine, bupivacaine, buprenorphine, butacaine, butethamate, chlorcyclizine, chlorpheniramine, chlorphenoxamine, chlorprenaline, chlorprothixene, cimetidine, cinchonidine, cinnarizine, clemastine, clomipramine, clonidine, cocaine, cyclazocine, cyclizine, cyclopentamine, cyproheptadine, deserpidine, desipramine, dextromoramide, dextropropoxyphene, dicyclomine, diethylcarbamazine, diethylpropion, diethylthiambutene, dihydroergotamine, dimethindene, dimethothiazine, diphenhydramine, diphenoxylate, dipipanone, diprenorphine, dipyridamole, disopyramide, dothiepin, doxapram, doxepin, doxylamine, droperidol, ephedrine, ergocornine, ergocristine, ergocristinine, ergocryptine, ergometrine, ergosine, ergosinine, ergotamine, ethopropazine, etorphine, etoxeridine, fenethazine, fenfluramine, fenoterol, fentanyl, flavoxate, fluopromazine, flupenthixol, fluphenazine, flunarazepam, haloperidol, hydroxyzine, hyoscine, ibogaine, imipramine, indapamine, iprindole, isothipendyl, isoxsuprine, ketanserine, laudanosine, lidocaine, lofepramine, loxapine, maprotiline, mecamlamine, meclophenoxate, meclozine, medazepam, mephentermine, mepivacaine, meptazinol, mepyramine, mesoridazine, metaraminol, methadone, methamphetamine, methapyrilene, methdilazene, methotrimeprazine, methoxamine, methoxyphenamine, methoxypromazine, methylephedrine, methylergonovine, methysergide, metoclopramide, metopimazine, metoprolol, mianserin, morazone, nadolol, nalorphine, naloxone, naphazoline, nicotine, nifedipine, nomifensine, nortriptyline, noscapine, orphenadrine, oxeladin, oxprenolol, oxymetazolin, papaverine, pargyline, pecazine, penbutolol, pentazocine, penthienate, pericyazine, perphenazine, phenadoxone, phenampromide, phenazocine, phenbutrazate, phendimetrazine, phenelzine, phenylglutarimide, phenindamine, pheniramine, phenmetrazine, phenomorphan, phenoperidine, phenothiazine, phenoxylbenzamine, phentolamine, phenylephrine, phenyltoloxamine, physostigmine, piminodine, pimozone, pindolol, pipamazine, pipazethate, piperacetazine, piperidolate, pipradol, pirenzepine, piritramide, pizotifen, practolol, pramoxine, prazosin, prenylamine, prilocaine, primaquine, proadifen,

procainamide, procaine, prochlorperazine, procyclidine, proheptazine, prolintane, promazine, promethazine, pronethalol, properidine, propiomazine, propranolol, prothipendyl, protriptyline, proxymetacaine, pseudoephedrine, pyrimethamine, quinidine, quinine, ranitidine, rescinnamine, sotalol, tacrine, terazosin, terbutaline, terfenadine, thenyldiamine, theophylline, thiethylperazine, thiopropazate, thioproperazine, thioridazine, thiothixene, thonzylamine, timolol, tocinide, tolpropamine, tolycaine, tranlycypromine, trazodone, trifluoperazine, trifluoperidol, trimeperidine, trimeprazine, trimethobenzamide, trimethoprim, trimipramine, tripeleminamine, triprolidine, tryptamine, verapamil, xylometazoline

REFERENCE

Jane, I.; McKinnon, A.; Flanagan, R.J. High-performance liquid chromatographic analysis of basic drugs on silica columns using non-aqueous ionic eluents. II. Application of UV, fluorescence and electrochemical oxidation detection, *J.Chromatogr.*, **1985**, 323, 191–225.

SAMPLE

Matrix: solutions

Sample preparation: Dissolve in MeOH:water 1:1 at a concentration of 50 µg/mL, inject a 10 µL aliquot.

HPLC VARIABLES

Column: 300 × 3.9 10 µm µBondapak C18

Mobile phase: MeOH:acetic acid:triethylamine:water 70:1.5:0.5:28

Flow rate: 1.5

Injection volume: 10

Detector: UV 254

CHROMATOGRAM

Retention time: 8

OTHER SUBSTANCES

Simultaneous: mesoridazine, promethazine, acetophenazine, thioridazine, prochlorperazine, butaperazine, thiethylperazine

REFERENCE

Roos, R.W.; Lau-Cam, C.A. General reversed-phase high-performance liquid chromatographic method for the separation of drugs using triethylamine as a competing base, *J.Chromatogr.*, **1986**, 370, 403–418.

SAMPLE

Matrix: solutions

Sample preparation: Prepare a 0.5 mg/mL solution in MeOH, inject a 5 µL aliquot.

HPLC VARIABLES

Column: 250 × 4.6 Zorbax RX

Mobile phase: Gradient. A was 150 mM phosphoric acid and 50 mM triethylamine. B was MeCN:water 80:20 containing 150 mM phosphoric acid and 50 mM triethylamine. A:B 100:0 for 2.2 min then to 0:100 over 30 min.

Column temperature: 30

Flow rate: 2

Injection volume: 5

Detector: UV 210

CHROMATOGRAM

Retention time: 18.9

OTHER SUBSTANCES

Simultaneous: acetaminophen, aprobarbital, butabarbital, chlordiazepoxide, chloroxylenol, clenbuterol, cortisone, danazol, diflunisal, doxapram, estrone, fluoxymesterone, mefenamic acid, methyltestosterone, nicotine, oxazepam, phentermine, phenylpropanolamine, progesterone, sulfamethazine, sulfanilamide, testosterone, testosterone propionate, tranquylpromine, tripeleppamine

KEY WORDS

details for purification of triethylamine in paper

REFERENCE

Hill,D.W.; Kind,A.J. The effects of type B silica and triethylamine on the retention of drugs in silica based reverse phase high performance chromatography, *J.Liq.Chromatogr.*, **1993**, *16*, 3941-3964.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Guard column: 30 × 2.1 Spheri-5 RP-8

Column: 220 × 2.1 Spheri-5 RP-8

Mobile phase: Gradient. A was 0.08% diethylamine and 0.09% phosphoric acid in water, pH 2.3. B was MeCN:water 90:10 containing 0.08% diethylamine and 0.09% phosphoric acid. A:B 95:5 for 2 min, to 0:100 over 15 min (?), maintain at 0:100 for 5 min.

Column temperature: 50

Flow rate: 0.5

Detector: UV 200

CHROMATOGRAM

Retention time: 15

OTHER SUBSTANCES

Simultaneous: mesoridazine, promazine, thiothixene, trifluoperazine, thioridazine

Also analyzed: amitriptyline, amphetamine, chlordiazepoxide, desalkylflurazepam, desipramine, desmethyldoxepin, diazepam, diethylpropion, doxepin, ephedrine, fenfluramine, flurazepam, imipramine, methamphetamine, norchlordiazepoxide, nordiazepam, nortriptyline, oxazepam, phentermine, phenylpropanolamine, prazepam

REFERENCE

Rainin Catalog, C1-94, **1994**, p. 7.24.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4.6 Zorbax RX

Mobile phase: Gradient. A was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 1 L water. B was 10 mL concentrated orthophosphoric acid and 7 mL triethylamine in 200 mL water, make up to 1 L with MeCN. A:B from 100:0 to 0:100 over 30 min, maintain at 0:100 for 5 min.

Column temperature: 30

Flow rate: 2

Detector: UV 210

OTHER SUBSTANCES

Also analyzed: acepromazine, acetaminophen, acetophenazine, albuterol, aminophylline, amitriptyline, amobarbital, amoxapine, amphetamine, amylocaine, antipyrine, aprobarbital, aspirin, atenolol, atropine, avermectin, barbital, benzocaine, benzoic acid, benzotropine, benzphetamine, berberine, bibucaine, bromazepam, brompheniramine, buprenor-

phine, buspirone, butabarbital, butacaine, butethal, caffeine, carbamazepine, carbromal, chloramphenicol, chlordiazepoxide, chloroquine, chlorothiazide, chloroxylenol, chlorphenesin, chlorpropamide, chlortetracycline, cimetidine, cinchonidine, cinchonine, clenbuterol, clonazepam, clonixin, clorazepate, cocaine, codeine, colchicine, cortisone, coumarin, cyclazocine, cyclobenzaprine, cyclothiazide, cyheptamide, cymarin, danazol, danthron, dapsone, debrisoquine, desipramine, dexmethasone, dextromethorphan, dextropropoxyphene, diamorphine, diazepam, diclofenac, diethylpropion, diethylstilbestrol, diflunisal, digitoxin, digoxin, diltiazem, diphenhydramine, diphenoxylate, diprenorphine, dipyrone, disulfiram, dopamine, doxapram, doxepin, dronabinol, ephedrine, epinephrine, epinine, estradiol, estriol, estrone, ethacrynic acid, ethosuximide, etonitazene, etorphine, eugenol, flamotidine, fenbendazole, fencamfamine, fenpropfen, fenproporex, fentanyl, flubendazole, flufenamic acid, flunitrazepam, 5-fluorouracil, fluoxymesterone, fluphenazine, furosemide, gentisic acid, gitoxigenin, glipizide, glunixin, glutethimide, glybenclamide, guaiaacol, halazepam, haloperidol, hydrochlorothiazide, hydrocodone, hydrocortisone, hydromorphone, hydroxyquinoline, ibogaine, ibuprofen, iminostilbene, imipramine, indomethacin, isocarboxtyril, isocarboxazid, isoniazid, isoproterenol, isoxsuprine, ivermectin, ketamine, keto-profen, kynurenic acid, levorphanol, lidocaine, lorazepam, lormetazepam, loxapine, mazindol, mebendazole, meclizine, meclofenamic acid, medazepam, mefenamic acid, megestrol, mepacrine, mepiridine, mephentermine, mephénytoin, mephesin, mephobarbital, mepivacaine, mescaline, mesoridazine, methadone, methamphetamine, methapyrilene, methaqualone, methazolamide, methocarbamol, methoxamine, methsuximide, methyl salicylate, methyl dopa, methyl dopamine, methylphenidate, methylprednisolone, methyltestosterone, methypylon, metoprolol, mibolerone, morphine, nadolol, nalorphine, naloxone, naltrexone, naphazoline, naproxen, nefopam, niacinamide, nicotine, niacin, nifedipine, niflumic acid, nitrazepam, norepinephrine, nortriptyline, noscapine, nyldrin, oxazepam, oxycodone, oxymorphone, oxyphenbutazone, oxytetracycline, papaverine, pargyline, pemoline, pentazocine, pentobarbital, persantine, phenacetin, phenazocine, phenazopyridine, phencyclidine, phendimetrazine, phenelzine, pheniramine, phenobarbital, phenothiazine, phensuximide, phentermine, phenylbutazone, phenylephrine, phenylpropanolamine, piperocaine, prazepam, prednisolone, primidone, probenecid, progesterone, propiomazine, propranolol, propylparaben, pseudoephedrine, puromycin, pyrilamine, pyrithyldione, quazepam, quinaldic acid, quinidine, quinine, ranitidine, recinnamine, reserpine, resorcinol, saccharin, albuterol, salicylamide, salicylic acid, scopolamine, scopoletin, secobarbital, strychnine, sulfacetamide, sufadiazine, sulfadimethoxine, sulfaethidole, sulfamerazine, sulfamethazine, sulfamethoxizole, sulfanilamide, sulfapyridine, sulfasoxizole, sulindac, tamoxifen, temazepam, testosterone, tetracaine, tetracycline, tetramisole, thebaine, theobromine, theophylline, thiabendazole, thiamine, thiamylal, thiobarbituric acid, thioridazine, thiosalicylic acid, thiothixene, thymol, tolazamide, tolazoline, tobutamide, tolmetin, tranlycypromine, triamcinolone, tribenzylamine, trichloromethiazide, trifluoperazine, trihexyphenidyl, trimethoprim, tripeleennamine, triprolidine, tropacocaine, tyramine, verapamil, vincamine, warfarin, yohimbine, zoxazolamine

REFERENCE

Hill, D.W.; Kind, A.J. Reversed-phase solvent gradient HPLC retention indexes of drugs, *J. Anal. Toxicol.*, **1994**, *18*, 233–242.

SAMPLE

Matrix: solutions

HPLC VARIABLES

Column: 250 × 4.6 5 µm Supelcosil LC-DP (A) or 250 × 4 5 µm LiChrospher 100 RP-8 (B)
Mobile phase: MeCN:0.025% phosphoric acid:buffer 25:10:5 (A) or 60:25:15 (B) (Buffer was 9 mL concentrated phosphoric acid and 10 mL triethylamine in 900 mL water, adjust pH to 3.4 with dilute phosphoric acid, make up to 1 L.)

Flow rate: 0.6

Injection volume: 25

Detector: UV 229

CHROMATOGRAM**Retention time:** 17.00 (A), 7.75 (B)**OTHER SUBSTANCES**

Also analyzed: acebutolol, acepromazine, acetaminophen, acetazolamide, acetophenazine, albuterol, alprazolam, amitriptyline, amobarbital, amoxapine, antipyrine, atenolol, atropine, azatadine, baclofen, benzocaine, bromocriptine, brompheniramine, brotizolam, bupivacaine, buspirone, butabarbital, butalbital, caffeine, carbamazepine, cetirizine, chlorcyclizine, chlordiazepoxide, chlormezanone, chloroquine, chlorpheniramine, chlorpromamide, chlorprothixene, chlorthalidone, chlorzoxazone, cimetidine, cisapride, clomipramine, clonazepam, clonidine, clozapine, cocaine, codeine, colchicine, cyclizine, cyclobenzaprine, dantrolene, desipramine, diazepam, diclofenac, diflunisal, diltiazem, diphenhydramine, diphenidol, diphenoxylate, dipyrindamole, disopyramide, dobutamine, doxapram, doxepin, droperidol, encainide, ethidium bromide, ethopropazine, fenopropfen, fentanyl, flavoxate, fluoxetine, fluphenazine, flurazepam, flurbiprofen, flvoxamine, furosemide, glutethimide, glyburide, guaifenesin, haloperidol, homatropine, hydralazine, hydrochlorothiazide, hydrocodone, hydromorphone, hydroxychloroquine, hydroxyzine, ibuprofen, imipramine, indomethacin, ketoconazole, ketoprofen, ketorolac, labetalol, levorphanol, lidocaine, loratadine, lorazepam, lovastatin, loxapine, mazindol, mefenamic acid, meperidine, mephénytoin, mepivacaine, mesoridazine, metaproterenol, methadone, methdilazine, methocarbamol, methotrexate, methotrimeprazine, methoxamine, methyl-dopa, methylphenidate, metoclopramide, metolazone, metoprolol, metronidazole, midazolam, moclobemide, morphine, nadolol, nalbuphine, naloxone, naphazoline, naproxen, nifedipine, nizatidine, norepinephrine, nortriptyline, oxazepam, oxycodone, oxymetazoline, paroxetine, pemoline, pentazocine, pentobarbital, pentoxifylline, perphenazine, pheniramine, phenobarbital, phenol, phenolphthalein, phentolamine, phenylbutazone, phenyltoloxamine, phenytoin, pimizide, pindolol, piroxicam, pramoxine, prazepam, prazosin, probenecid, procainamide, procaine, prochlorperazine, procyclidine, promazine, promethazine, propafenone, propantheline, propiomazine, propofol, propranolol, protriptyline, quazepam, quinidine, quinine, racemethorphan, ranitidine, remoxipride, risperidone, salicylic acid, scopolamine, secobarbital, sertraline, sotalol, spironolactone, sulfonpyrazone, sulindac, temazepam, terbutaline, terfenadine, tetracaine, theophylline, thiethylperazine, thiopental, thioridazine, thiothixene, timolol, tocanide, tolbutamide, tolmetin, trazodone, triamterene, triazolam, trifluoperazine, trifluopromazine, trimeprazine, trimethoprim, trimipramine, verapamil, warfarin, xylometazoline, yohimbine, zopiclone

KEY WORDS

also details of plasma extraction

REFERENCE

Koves, E.M. Use of high-performance liquid chromatography-diode array detection in forensic toxicology, *J.Chromatogr.A*, **1995**, *692*, 103–119.

SAMPLE**Matrix:** solutions**Sample preparation:** Inject a 50-200 μ L aliquot of a solution in pH 7.4 Tyrode's buffer.**HPLC VARIABLES****Column:** 150 \times 3.9 μ m Nova-Pak C-18**Mobile phase:** MeCN:50 mM phosphoric acid:triethylamine 40:60:0.1**Column temperature:** 35**Flow rate:** 0.6**Injection volume:** 50-200**Detector:** UV 230**OTHER SUBSTANCES****Also analyzed:** propantheline, verapamil

KEY WORDS

buffer

REFERENCE

Saitoh,H.; Aungst,B.J. Possible involvement of multiple P-glycoprotein-mediated efflux systems in the transport of verapamil and other organic cations across rat intestine, *Pharm.Res.*, **1995**, *12*, 1304–1310.

SAMPLE

Matrix: solutions

Sample preparation: Inject a 20 μ L aliquot of a 25 ng/mL solution in pH 4.0 acetate/citrate buffer.

HPLC VARIABLES

Column: 150 \times 0.32 3 μ m Hypersil C18

Mobile phase: MeCN:pH 4.0 acetate/citrate buffer 45:55

Injection volume: 20

Detector: UV

CHROMATOGRAM

Retention time: 12

OTHER SUBSTANCES

Simultaneous: methotrimeprazine (levomepromazine), thioridazine

KEY WORDS

microcolumn

REFERENCE

Streel,B.; Ceccato,A.; Chiap,P.; Hubert,P.; Crommen,J. Injection-generated solvent and pH gradients for sample enrichment on injection of large volumes in microcolumn liquid chromatography, *Bio-med.Chromatogr.*, **1995**, *9*, 254–256.

SAMPLE

Matrix: solutions

Sample preparation: Inject a 20 μ L aliquot of a 100-500 μ g/mL solution in mobile phase.

HPLC VARIABLES

Column: 100 \times 4.6 5 μ m Hypersil C8 MOS 100A coated with phosphatidylcholine (95% pure soybean lecithin, Epikuron, Lucas Meyer & Co.) (Coat column by recycling a 1 mM solution of phosphatidylcholine in MeOH:water 80:20 for 24 h.)

Mobile phase: MeCN:35 mM pH 7.4 sodium phosphate buffer 40:60

Flow rate: 0.5–2

Injection volume: 20

Detector: UV 254

CHROMATOGRAM

Retention time: k' 10.23

OTHER SUBSTANCES

Also analyzed: amoxicillin, antipyrine, carbamazepine, chlorpheniramine, clonidine, codeine, desipramine, diphenhydramine, dipyridamole, ephedrine, flufenamic acid, haloperidol, hydroxyzine, imipramine, indomethacin, lidocaine, megestrol acetate, metoprolol, nabumetone, nadolol, phenobarbital, phenol, promazine, propranolol, pyrilamine, quinidine, ropinirole, testosterone, thioridazine, tolfenamic acid, verapamil

Noninterfering: acetaminophen, aspirin, azathioprine, caffeine, carprofen, chlorambucil, cimetidine, fenoterol, flurbiprofen, ibuprofen, ketoprofen, ranitidine, salicylic acid, sulfamethoxazole, theophylline, thioguanine, tiaprofenic acid, trimethoprim, valproic acid

KEY WORDS

comparison with capillary electrophoresis

REFERENCE

Hanna,M.; de Biasi,V.; Bond,B.; Salter,C.; Hutt,A.J.; Camilleri,P. Estimation of the partitioning characteristics of drugs: A comparison of a large and diverse drug series utilizing chromatographic and electrophoretic methodology, *Anal.Chem.*, **1998**, 70, 2092–2099.

SAMPLE

Matrix: tissue

Sample preparation: Condition a Sep-Pak C18 SPE cartridge with 5 mL MeOH and 5 mL water. Homogenize kidney with a kitchen grinder. Weigh out a 5 g sample and add 20 mL MeCN with continuous gentle mixing, mix vigorously on a vibromixer at 1500 rpm for 30 s, sonicate for 2 min, centrifuge at 4000 g for 5 min. Mix 7.5 mL sample extract and 40 mL 10% NaCl and add to SPE cartridge, wash with 1 mL 10 mM sulfuric acid, wash with 2 mL air, elute with 2 mL acidic MeCN. Place eluate in a washed tube and evaporate to 300 μ L at 70° under a stream of nitrogen, mix gently, add 1 mL n-hexane, mix on a vibromixer for 30 s, centrifuge at 2000 g, inject a 50 μ L aliquot of the aqueous phase. (Acidic MeCN was 1 mL 50 mM sulfuric acid and 100 mL MeCN. The washed tube was prepared by rinsing with concentrated ammonia, water, and acetone and drying under a stream of nitrogen.)

HPLC VARIABLES

Guard column: 10 \times 2.1 37-50 μ m Bondapak C18

Column: 300 \times 3.9 Bondapak C18

Mobile phase: MeCN:water 55:45 containing 2.46 g/L anhydrous sodium acetate, pH adjusted to 6.5 with acetic acid

Flow rate: 1.2

Injection volume: 50

Detector: UV 240

CHROMATOGRAM

Retention time: 25

Limit of detection: 6 ng/g

OTHER SUBSTANCES

Extracted: azaperol, carazolol, acepromazine, xylazine, azaperone, haloperidol, propiomazine

KEY WORDS

SPE; pig; kidney

REFERENCE

Keukens,H.J.; Aerts,M.M.L. Determination of residues of carazolol and a number of tranquilizers in swine kidney by high-performance liquid chromatography with ultraviolet and fluorescence detection, *J.Chromatogr.*, **1989**, 464, 149–161.

SAMPLE

Matrix: tissue

Sample preparation: Condition a Bond-Elut C18 SPE cartridge with 5 mL MeOH and 5 mL water. Cut pig kidney or liver into small pieces and homogenize. 5 g Homogenate + 10 mL MeCN, shake, vortex for 30 s, sonicate for 3 min, vortex for 30 s, sonicate for 3 min, centrifuge at 10000 g for 20 min. Add 7.5 mL supernatant + 40 mL 10% NaCl to

the SPE cartridge at about 1 mL/min, do not allow cartridge to dry out, wash with 850 μ L 10 mM sulfuric acid, dry with air, elute with 3.5 mL acidic MeCN. Evaporate the eluate to dryness under a stream of nitrogen at 50°, reconstitute the residue in 300 μ L 10 mM sulfuric acid, vortex briefly, add 1 mL hexane, vortex for 30 s, centrifuge at 2000 g for 5 min, inject an aliquot of the aqueous layer. (Acidic MeCN was 1 mL 50 mM sulfuric acid in 100 mL MeCN.)

HPLC VARIABLES

Guard column: Hypersil 5 μ m SAS C1

Column: 250 mm long 5 μ m Hypersil SAS C1

Mobile phase: MeCN:water 50:50 containing 0.77 g/L ammonium acetate

Flow rate: 2

Detector: E, ESA Model 5100A Coulochem, first electrode +0.4 V, second electrode (which was monitored) +0.7 V, Model 5020 guard cell after pump but before injector at +0.75 V

CHROMATOGRAM

Retention time: 32

Limit of detection: 2 ng/g

OTHER SUBSTANCES

Extracted: azaperol, acepromazine, carazolol, azaperone, xylazine, haloperidol, propiomazine

KEY WORDS

SPE; pig; kidney; liver

REFERENCE

Rose, M.D.; Shearer, G. Determination of tranquilisers and carazolol residues in animal tissue using high-performance liquid chromatography with electrochemical detection, *J. Chromatogr.*, **1992**, 624, 471–477.